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A MICROSCOPICAL STUDY OF THE SPINAL CORD IN TWO CASES OF POTT'S DISEASE.*

By William G. Spiller, M. D., *Professor of Diseases of the Nervous System in the Philadelphia Polyclinic; Associate in the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania.*

[*From the William Pepper Laboratory of Clinical Medicine.*]

We have learned much about spinal caries since Percival Pott† wrote his work on this disease so many years ago, but we have not exhausted the subject, and it is still one of much interest.

The two cases which I have the honor to present for your consideration represent two forms of the affection, an early and a late; one in which the cord has not been compressed by displaced vertebræ, and one—and rather a rare variety—in which the cord has been almost severed as the result of such displacement in connection with an extradural tuberculous abscess.

The cause of the compression is only mentioned in thirty-nine of the fifty-two cases of paralysis from spondylitis which Schmaus collected from the literature;‡ in thirty-three of these a caseous pachymeningitis was noted; in six the compression was caused by dislocation of the vertebræ, and in five of these six the odontoid process of the axis was dislocated. Therefore only in one of thirty-nine cases the compression was due to kyphotic displacement. Kraske* adds to this number and shows that only in one case out of fifty-two was the compression of the cord due to deviation of the vertebræ alone (omitting the five cases above mentioned). He tells us that only in about two per cent. of the cases the paralysis from spondylitis is caused by kyphosis alone; in all the rest it is due to compression from a peripachymeningitic exudate.

The case B. H. is, therefore, one of considerable interest, for the compression was chiefly due to displaced vertebræ, though there was also a peripachymeningitis.

The first case—for which I am indebted to Dr. Willard and Dr. Lloyd—was in a boy of about twelve years of age. Dr. Lloyd, who frequently saw the patient during his lifetime, told me that the boy had complained of great pain in the region of a cervico-thoracic kyphosis. He was not paralyzed. Before death dyspnœa became intense, and Dr. Lloyd believed

* Read by invitation before the Johns Hopkins Hospital, January 17th, 1898.

† Pott, Remarks on that kind of palsy of the lower limbs which is frequently found to accompany a curvature of the spine, etc. The Chirurgical Works of Percival Pott, F. R. S., Vol. III.

‡ Die Compression-Myelitis bei Caries der Wirbelsäule. Wiesbaden, 1890. J. F. Bergmann. Quoted by Kraske.

* Kraske, Archiv für klin. Chirurgie, Vol. XLI.

that death was due to paralysis of the respiratory muscles. This was possibly the result of intense round cell infiltration of the cord in the mid-cervical region where the phrenic nerve has its origin.

The report of the necropsy is as follows: The body was that of a much emaciated boy. Kyphosis was present without scoliosis, and the prominence was at the fifth, sixth, seventh cervical and first thoracic vertebræ, and was greatest at the junction of the seventh cervical with the first thoracic. Much pus was found within the cervical portion of the vertebral canal, external to the dura. The dura was adherent by its anterior surface to the bodies of the seventh cervical and first thoracic vertebræ, and a cheesy, fibrous mass was observed on its ventral and external surface. The bodies of the lower cervical and first thoracic vertebræ were carious and yielded to slight pressure from a blunt instrument. No tuberculous lesions were found elsewhere.

The spinal cord was not compressed and secondary degeneration was not noted. The chief interest of this case lies in the fact that it shows the earlier stages of Pott's disease—whereas the following case shows the late—and presents a very intense round cell infiltration of the meninges and cord, without specific signs of a tuberculous process interior to the dura. Such signs are, however, very abundant in the mass external to the dura. The dura has acted to some degree as a barrier, but it also shows some round cell infiltration. Along the periphery of the lateral columns in the upper thoracic region spaces are found from which the nerve fibres have disappeared, and in some sections a few swollen axis cylinders are seen. There is very distinct perivascular infiltration of round cells within the cord; this is well marked at the mid-cervical region and involves the vessels of all parts of the transverse area, and is noticed also within the anterior horns. The perivascular infiltration is especially noticeable at this level, about the vessels of the anterior fissure and posterior septum. In the posterior columns of the mid-cervical region necrotic areas are seen, which stain faintly with Weigert's hæmatoxylin solution and show a diminution in the number of nerve fibres. When the carmine and Delafield's hæmatoxylin are used, moderate round cell infiltration, some proliferation of neuroglia, and some slight swelling of the axis cylinders are noticed in these areas. This necrosis is probably dependent on the vascular condition. No other necrotic areas have been noticed within the cord. The motor cells of the mid-cervical region do not appear greatly altered, but unfortunately the method of Nissl could not be used. In the first and second cervical segments the infiltration is much less in intensity, but it is very distinct in the lumbar region, where the vessels are also much dilated.

The anterior roots in the upper thoracic region are greatly degenerated, but the posterior have partially escaped. The motor cells in this portion of the cord are distinctly altered. The Marchi stain does not reveal degenerated fibres.

In the mass external to the dura many giant cells, large collections of round and epithelioid cells, and caseous areas are found.

The second case, for which I am indebted to Dr. Willard, is as follows: The child, B. H., came of a tuberculous family and suffered from bronchitis every winter. The evidences of Pott's disease first appeared when the patient was three years of age. She complained of pain in the back, and kyphosis was soon afterward noticed. About four months after the first evidences of the disease were detected the child was found to be liable to fall without sufficient cause. A year later the tendons of both heels were operated on, a fact which shows that the disease progressed rapidly. At eight years of age prominence of the first, second and third thoracic vertebræ, atrophy of the legs with paralysis, contracture of the hamstring tendons, and large sores over the hip-joints were noticed. The child died when eight years old; the process, therefore, lasted five years. It is stated that she had had no power of motion in the legs and no control of the bladder, although rectal disturbance had not been noted.

When the vertebral column was examined at the necropsy the body of the seventh cervical vertebra was found almost at a right angle with that of the first thoracic. The latter was carious and yielded to slight pressure from a blunt instrument. Permission was not obtained to remove any of the bony part of the spinal column, and more careful examination of the vertebræ could not be made. The cord was very small in the region corresponding to the prominence made by the first thoracic with the seventh cervical vertebra, and had evidently very little space for growth. The unusual degree of compression was possibly the result of the development of the Pott's disease at the early age of three years. Segments an inch above or below the seat of compression were much larger. The compressed portion was soft and was removed with difficulty. A cheesy fibrous mass was found adherent to the external and right side of the dura, extending downward about an inch, and upward about half an inch from the compressed region, and together with the displaced vertebræ had caused the signs of compression. The dura was not adherent to the cord, and no evidence of internal meningitis was present.

Dr. Sailer examined the thoracic and abdominal viscera and found areas of pneumonic infiltration in the stage of red hepatization in the middle lobe of the right lung and in the lower part of the upper lobe of the left.

After the spinal cord had been hardened it was examined microscopically. In the region of greatest compression, at the cervico-thoracic junction of the vertebræ, the cord contains very few medullated fibres, and even those present are most irregularly arranged. It is impossible to make any distinction between gray and white matter. The vessels within the cord are sclerosed. Numerous nuclei, both round and elongated, are found in all parts of the sections, and some of these probably represent a round cell infiltration. No nerve cells are observed. The pia is much thickened and contains altered blood pigment. Both anterior and posterior roots external to the cord are in a fairly good state of preservation. The vessels within the cord stand out prominently from the surrounding tissue as faintly stained pink patches when the carmine is used, and as pale yellow ones with Weigert's hæmatoxylin. The central canal is closed at this portion of the cord.

Sections two to three root segments above the area of greatest compression show the central canal quite widely open. There is little round cell infiltration. The columns of Goll,

with the exception of a few fibres along their periphery, are greatly degenerated. These few normal fibres have probably escaped destruction at the area of compression. A few scattered normal fibres are found also in other parts of these columns. Normal fibres from the posterior commissure are distinctly seen passing into the degenerated columns of Goll. Burdach's columns also are not free from degeneration. The direct cerebellar tracts and columns of Gowers are much degenerated, but just below the motor decussation many medullated fibres may be seen within the former; it would seem, therefore, that these tracts are partly formed by nerve fibres whose cells are situated above the lower cervical region, or that—and this is more probable—fibres of the crossed pyramidal tracts are more intimately mingled with those of the direct cerebellar tracts at this level. Very distinct ascending degeneration of the lateral columns in the area of the crossed pyramidal tracts is noted, and this extends through several root segments and gradually disappears above the mid-cervical region. The direct pyramidal tracts show an ascending degeneration of less intensity.

Below the compressed area the horns of the cord gradually assume their normal form, and medullated fibres first appear nearest the gray matter and gradually increase in extent toward the periphery. The crossed pyramidal, Gowers', and the direct cerebellar tracts are greatly degenerated, and the direct pyramidal is also involved. Very few medullated fibres are found in the area of the lateral motor tracts below and near the region of compression, and though the number of these increases as lower levels of the cord are examined, they are never as abundant as one might expect. There are, therefore, associative fibres within the crossed pyramidal tracts, but their number is limited.

In the lateral columns the degeneration extends considerably in advance of that marked out as the area of the lateral motor columns by secondary degeneration from cerebral lesions. Degeneration of the peripheral part of the anterior columns near the anterior fissure may be traced well into the mid-lumbar region.

The central canal is enlarged both above and below the cervico-thoracic junction, and in the lumbar region is surrounded by so much gliar tissue that it almost resembles the condition frequently seen in syringomyelia. Very distinct degeneration is seen in the posterior columns below the area of compression, not limited to Schultze's comma zones, and involving most of the transverse area of the posterior columns, except at their periphery, where the long neurones from the lumbo-sacral cord are found. This degeneration may be traced fully three and a half to four centimetres below the compressed portion of the cord.

The cells of the anterior horns in the lumbar cord appear to be normal both in shape and number, but Clarke's columns are entirely deprived of cells throughout their extent in the thoracic region, and in the upper part of the lumbar cord, where they contain normally very many cells, they present the usual form but are without cells. The fibres within these columns from the posterior roots are normal in number. Careful search may possibly reveal here and there an atrophied cell in these columns.

This is evidently a case in which compression has played the chief rôle, but there is some round cell infiltration about the vessels of the pia and certain of those of the cord as far as the lower thoracic region.

The Marchi stain reveals degenerated fibres scattered all over the transverse area of the cord below the compression, but these are most numerous in the anterior columns.

The ascending degeneration in the pyramidal tracts, both crossed and direct, observed in the case B. H., is worthy of mention. In the crossed pyramidal tract this is more distinct than in the direct, and extends through several cervical segments. This retrograde degeneration has formed the subject of study in a number of cases, and in 1896, in the American Journal of the Medical Sciences, Dercum and Spiller gave the literature on the subject so far as they were able to obtain it. It has been explained by some writers, and especially by Sottas, as an upward degeneration in motor fibres which, of course, conduct impulses downward; by others it has been thought to be an involvement of associative fibres—of fibres which arise within the spinal cinerea, pass out into the lateral column and terminate within the cinerea at higher levels. In favor of the first view is the fact that it is found usually in processes of long duration, for I am unaware that it has been described as occurring in any acute process, which we should expect would be the case if it is merely a cellulifugal degeneration. Then again, when the remaining part of the lateral column and the crossed pyramidal tract are degenerated the process often does not extend so far upward in the former as in the latter. Thus Hoche* mentions degeneration of fibres in the lateral column, not belonging to any known system, extending through three segments above the focal lesion, and of the crossed pyramidal tract extending through seven segments. It is not easy to explain this on the assumption that longer associative fibres are found in the crossed pyramidal tract than in the remaining part of the lateral column. "The law of the excentric position of the long tracts in the spinal cord" (Flatau, Zeitschrift f. klin. Med., Vol. XXXIII, Nos. 1 and 2), which simply means that the long fibres take a peripheral and posterior location, might possibly be used as an argument. Egger† explains the retrograde degeneration of the crossed pyramidal tracts, observed in his case, by the theory that it represented short fibres, and that sclerosis occurred when these fibres were degenerated, and that this in turn caused degeneration of the long pyramidal fibres. I have several times observed this retrograde degeneration of the motor tracts and am convinced that it is more common than is usually supposed. In my case B. H. the normal fibres in the crossed pyramidal tract below and near the focal lesion are not numerous. Below the transverse lesion these ascending associative fibres, having their origin in the spinal cinerea, should not be affected, and they should be in normal number, if retrograde degeneration is to be discarded. If we grant that retrograde degeneration may occur in associative fibres, we should be at a loss to explain why the pyramidal fibres are not subject to the same laws, and we must

* Hoche, Archiv für Psychiatrie, Vol. XXVIII, 1896.
† Egger, Archiv für Psychiatrie, Vol. XXVII.

grant the possibility of this form of degeneration in order to explain the degeneration of the direct cerebellar tracts below the transverse lesion in this case.

In the direct pyramidal tracts the degeneration possibly is confined to Marie's* sulco-marginal zones, but does not extend very far upward. I know of no way in which the question as to whether it involves associative fibres here, or fibres of the direct motor tracts, may be settled. These areas may degenerate upward for a long distance. Hoche (*l. c.*), for instance, has traced this degeneration from a lesion in the mid-thoracic region into the motor decussation, and Dercum and Spiller (*l. c.*) traced it from the upper thoracic region to the same point.

The degeneration of Gowers' tract below the lesion, which is observed in the case B. H., has been found also in other cases, and it seems to be generally held that this tract contains fibres which conduct impulses in both directions. Hoche (*l. c.*) in a case with a lesion of the mid-thoracic region found this bundle degenerated below the lesion as far as the lower lumbar cord. This is where many neuropathologists believe the bundle arises,—at a lower level than the direct cerebellar tract. Daxenberger† and others speak of descending degeneration of Gowers' tract.

The fact that fibres of the antero-lateral column not belonging to any known system degenerate only a few segments either above or below a transverse lesion of the cord has been observed in many cases. This may be well seen in the case B. H. The restoration of fibres in the antero-lateral column begins always nearest the cinerea, for these in this portion are short associative fibres, and the Grenzschicht of Flechsig is never degenerated through any great extent of the spinal cord. This is in conformity with "the law of the excentric position of the long tracts in the spinal cord." (Flatau, *l. c.*)

As a rule the comma zones of the posterior columns can only be traced a short distance by Weigert's stain, two, three or four segments, but when the Marchi method has been employed they have been followed much further. In the case B. H. they are not sharply separated from the degenerated fibres in the rest of the posterior columns, though the area occupied by them is possibly slightly paler by Weigert's stain. This generalized degeneration of the posterior columns seems to me well worthy of note, for it can be followed four centimetres below the focal lesion, through several segments, in portions of the cord in which the gray matter is apparently normal. It seems to be more extensive than that we are accustomed to speak of as the traumatic zone, for according to Schiefferdecker the traumatic degeneration extends above or below a focal lesion only about ½ to 1 cm. (quoted by Worotynski, Neurologisches Centralblatt, No. 23, 1897). I am inclined to regard this descending degeneration in the posterior columns as retrograde, if we have the right to use such a term for a process which is more one of atrophy than degeneration. It may be that the development of the compression at the early age of three years explains this condition, for we have been taught that the pyramidal fibres are not fully developed until the fourth year of extra-uterine life. We know that the fibres of the posterior columns receive their medullary sheaths quite early, but it is possible that at the third year of extra-uterine life—if we can believe that the compression of the cord in the case B. H. was already well developed at that period—these fibres are less resistant than they are later.

Similar diffuse descending degeneration in the posterior columns below the area of compression has been noticed in a case of Pott's disease by Fürstner. In his case the compression was at the level of the ninth thoracic vertebra. He describes the lesion as follows: "There is a degeneration in the posterior columns which is not very intense, but which may be traced into the lumbar region, and occupies almost the entire width of the posterior columns, with the exception of the peripheral portion of these columns and of the well known band of fibres which has its course parallel to the posterior horns." This degeneration of the posterior columns Fürstner* regarded as wider than that we not infrequently see in Schultze's comma zones.

Cellulipetal degeneration of sensory fibres has been considered a rare occurrence, and indeed I have seen the statement (Nageotte†) that retrograde intramedullary degeneration of posterior root fibres has never been observed. It would be difficult to explain the descending degeneration of the posterior columns as an involvement of the associative fibres, for v. Lenhossék‡ tells us that positively there are only a few cells in the posterior horns which send their axis cylinders into the posterior columns.

The descending degeneration of the direct cerebellar tracts has not been frequently mentioned, and the completeness of it in the case B. H. is possibly due to the early age of the patient at the time the destruction began. Strümpell,§ Daxenberger,‖ and Bischoff¶ have spoken of it, and Bischoff thinks it is possible that the destruction of the direct cerebellar tract in his case may have had a connection with the descending cerebellar fibres described by Biedl.** In his case the cells of Clarke's column were normal. Thomas,†† in lesions experimentally produced on the cerebellum in the dog, found atrophy of these cells. In Daxenberger's (*l. c.*) case also these cells were not normal in number and size, nor were they normal in Strümpell's (*l. c.*) case. I have, therefore, searched carefully for cells in Clarke's column in the case B. H. and have been unable to find them, even in the lumbo-thoracic segments, where normally they are most abundant. A very few atrophied cells may be found by diligent search. The fibres within Clarke's columns are normal in appearance, as we should expect them to be, inasmuch as most of them come

* Marie, Leçons sur les maladies de la moelle. Paris, 1892.

† Daxenberger, Deutsche Zeitschrift für Nervenheilkunde, Vol. IV.

* Fürstner, Archiv für Psychiatrie, Vol. XXVII.

† Nageotte, Revue Neurologique, 1895.

‡ v. Lenhossék, Der feinere Bau des Nervensystems. Second edition, p. 355.

§ Strümpell, Archiv für Psychiatrie, Vol. X.

‖ Daxenberger, Deutsche Zeitschrift f. Nervenheilkunde, Vol. IV.

¶ Bischoff, Wiener klin. Wochenschrift, No. 37, 1896.

** Biedl, Neurologisches Centralbl., 1895, p. 434.

†† Thomas, Le Cervelet. G. Steinheil, Paris, 1897.

from the posterior roots. This retrograde degeneration of sensory fibres—for we have every reason to believe that the direct cerebellar tract is sensory—extending even to the origin of the fibres within the cells of Clarke's column, is of considerable importance and has rarely been described. It is probably due to the fact that the destruction began when the patient was very young, for such complete cellular atrophy is far more common in the young, as many experimental lesions have shown. It is also possible that the cells of Clarke's column were altered by the "reaction at distance" before the fibres of the direct cerebellar tracts were entirely degenerated.

In the case B. H. the area of degeneration, representing the fibres of the crossed pyramidal tract, in its downward course passes toward the periphery of the cord, and in the lumbo-thoracic region occupies the external and posterior part of the lateral column. Normal fibres are found in the crossed pyramidal tract below the area of compression, but they are not nearly as numerous as I have been led to expect from similar lesions of this tract reported in the literature, though in my case B. H. the normal fibres within this tract are more numerous at low than at high levels of the thoracic cord. It has been frequently stated that degeneration of the crossed pyramidal tract, resulting from a cerebral lesion, is less extensive than that following a spinal lesion. It may be that fibres of cerebellar origin—Van Gehuchten's* cortico-ponto-cerebello-spinal tract—are added to the cortico-spinal tract, or that a system of fibres forming the anterior part of the crossed pyramidal tract arises in the thalamus, as v. Bechterew† has concluded from the investigations of Boyce and Sakowitsch and from a study of the greater area of the lateral motor tract as represented during its myelination, compared with the area as represented by degeneration from cerebral lesions.

It is unquestionably true that the degenerated area of the crossed motor tract in the case B. H. is greater than that we find after cerebral lesions, but this is also partly due to the fact that many associative fibres are destroyed. It is probable that some associative fibres are contained within the lateral motor tract, but I cannot believe, from the case B. H., that fibres which arise below the lower cervical segments and pass downward are very numerous within this tract.

There is no atrophy of the motor cells of the anterior horns in the lumbar region, although we should expect to find it in this case, if in any, on account of the early age at which the transverse lesion occurred. I have never been able to observe this atrophy of the cell body of the peripheral neurone resulting from a lesion of the central neurone, and confess that I have always been most skeptical regarding statements concerning its existence. Recently, however, Schaffer‡ has published some noteworthy observations of tertiary degeneration. It may be mentioned that Egger (*l. c.*) says that in his case the cells were less numerous in one anterior horn in the lumbar region. I am not questioning Egger's statement, but from repeated observation we know how likely one is to be misled in an investigation of this kind, for often in normal cords the cells in the two anterior horns are not equally numerous, and we have no standard of what constitutes a normal number of cells.

Bruns* found the crossed pyramidal tracts, especially the right, wonderfully well preserved below and near a transverse lesion, though they were not entirely normal; and the explanation he suggests is that the degeneration began in the peripheral end of these tracts and had not extended to the traumatic area within the space of about four months. In my case B. H., which had lasted five years, this difference in the degree of degeneration in the distal and more proximal portions of the pyramidal tracts is not observable.

The degeneration in the antero-lateral columns in Bruns' case was believed by the author to represent the fibres of the direct pyramidal tract, descending fibres of Gowers' column, fibres of the système descendant du zone sulco-marginale (Marie) or faisceau marginal (Löwenthal), fibres of the faisceau intermédiaire du cordon latéral (Löwenthal), and the descending cerebellar tract of Marchi. The latter has never been demonstrated in man (Thomas). These areas are degenerated in the case B. H., and they have been found altered by Westphal, Schultze, Tooth, Schmauss, Daxenberger (quoted by Bruns) and others in cases observed by them.

Bechterew† has recently shown that there is still another system in the inner portion of the anterior column of the cord, and that this system arises in the anterior part of the corpora quadrigemina. He gives no name to this or to his system anterior to the crossed pyramidal tract, and we may, perhaps, speak of them as the quadrigemino-spinal and the thalamo-spinal tracts.

Dr. Young states that the patellar reflex in the case B. H. was diminished. So much has been written on the loss of the reflexes in total transverse lesions situated high in the cord that I may simply refer to the excellent papers by Bastian,‡ Bruns,§ Egger,‖ Hoche,¶ Habel** and others. Bruns' case was the first in which the reflexes were lost, and the entire spinal cord, the roots of the cauda equina, and a number of nerves and muscles of the lower extremities were examined microscopically. The changes in the nerves and muscles were not of great importance and could not be used to explain the absence of the patellar reflex and the flaccidity of the paralysis.

The posterior roots in Bruns' (*l. c.*) case in the area of total traumatic degeneration were remarkably well preserved, but the anterior were totally degenerated. He gives no satisfactory explanation for this. In the first case reported in this

* Van Gehuchten, Journal de Neurologie et d'Hypnologie, 1897.

† v. Bechterew, Neurologisches Centralblatt, No. 23, 1897.

‡ Schaffer, Monatsschrift für Psychiatrie und Neurologie, Vol. II, No. 1.

* Bruns, Archiv für Psychiatrie, Vol. XXV, 1893.

† Bechterew, Neurolog. Centralbl. No. 23, 1897.

‡ Bastian, A Dictionary of Medicine, edited by Richard Quain, M. D., F. R. S., p. 1481. Medico-Chirurgical Transactions, published by the Royal Medical and Chirurgical Society of London, Vol. 73, p. 151.

§ Bruns, Archiv für Psychiatrie, XXV.

‖ Egger, Archiv für Psychiatrie, XXVII.

¶ Hoche, Archiv für Psychiatrie, XXVIII.

** Habel, Archiv für Psychiatrie, XXIX.

paper the posterior roots were less affected. This is probably due to the fact that the anterior roots were most exposed to pressure and the invasion of the tuberculous process, and shielded to some degree the posterior roots placed behind them.

Bischoff (*l. c.*) concluded from his examination of a case of Pott's disease that the root fibres which enter below the second thoracic segment do not form all of Goll's columns, inasmuch as the ventral and lateral portions of these columns in the cervical region are formed by fibres from higher segments and probably not by those from the thoracic region.

If this view of Bischoff, viz. that the ventral and lateral parts of Goll's column are formed by fibres of the cervical roots, is correct, we are not surprised that these are the portions which the cervical fibres occupy. We know that the higher the degeneration of the posterior roots extends, the greater is the degeneration of the ventral and lateral portions of the postero-median columns in the cervical region. Reference may be made to the two cases pictured in the author's digest on the pathology of tabes,* or to many other cases, in illustration of this point. But there is considerable evidence to show that above the sixth thoracic roots the column of Goll in man is fully formed. In Pfeiffer's† case in which the first and second thoracic roots, in Nageotte's‡ case in which certain fibres of the second and third posterior thoracic roots, in Marguliés'§ case in which the right sixth posterior thoracic root, and in Dejerine and Thomas'‖ case in which the eighth cervical and first thoracic roots were affected, the columns of Goll in the cervical region were not degenerated. Bischoff employed the method of Marchi, and his results were possibly more accurate than those of the above-mentioned cases in which the hæmatoxylin of Weigert was used.

The case B. H. bears on this subject. The transverse lesion is situated in the lower cervical and upper thoracic cord, and at the mid-cervical region the columns of Goll are degenerated as far as the posterior commissure and spread out against the commissure in the well known flask-like form. The columns of Burdach also show distinct degeneration, but just below the motor decussation (first to second cervical segments) the degeneration is almost entirely confined to the columns of Goll, and only along their lateral borders is a slight degeneration of the columns of Burdach. At this level the columns of Goll do not extend to the posterior commissure. The columns of Goll, as they are represented by the degenerated area in the sections from the case B. H., do not receive cervical fibres except from the lowest cervical roots, if they receive them from these.

In a paper read at the last meeting of the American Medical Association I¶ attempted to show that there is considerable evidence for the theory that tuberculosis of the cord and its membranes may appear in the form of simple meningomyelitis, without the presence of giant cells, miliary tubercles, or even detectable bacilli, especially if Müller's fluid has been used for hardening. I was led to this conclusion after the examination of a case of meningomyelitis, apparently due neither to syphilis nor tuberculosis, as far as specific lesions were concerned, in a person who had died from generalized tuberculosis.

When the idea that spinal tuberculosis might appear as simple meningomyelitis first presented itself to my mind I was not aware of the attention which this subject had received, and was therefore somewhat surprised by the results of my examination of the literature. I found that a number of writers hold that both syphilis and tuberculosis may appear as simple meningomyelitis. Oppenheim, for instance, says: "We observe in syphilitic and tuberculous persons a form of myelitis which neither clinically nor anatomically can be considered specific, and yet it must stand in some relation to the infectious process."*

In the examination of these two cases of Pott's disease I have not noticed any lesions interior to the dura which might be called specific. It hardly seems probable that any one would hesitate to call these two cases tuberculous, unless the question of the rare manifestation of syphilis in this form might arise. The caries of the vertebræ, the external pachymeningitis, the giant cells, the necrosis of tissue within the tubercles, the epithelioid cells, render the diagnosis of a tuberculous process very probable. Within the dura, especially in the first case, the meninges are infiltrated with round cells, some of the vessels show a distinct endarteritis, round cell infiltration may be found about certain vessels within the cord, and in the first case several foci of degeneration may be noticed in the posterior columns at a considerable distance above the point of compression. A nuclear stain shows that these foci are the seat of a slight round cell infiltration. Within the dura, therefore, at least in one of these two cases of tuberculous spondylitis, only the signs of an ordinary meningomyelitis are present, even at some little distance from the seat of compression. Indeed in this first case the compression was so slight that it did not produce ascending or descending degeneration. The action of bacterial products on the cord need cause no surprise. We have had numerous experiments on this subject, and in this country Welch† and Flexner‡ have done much to enlighten us.

It is not clearly proven that the tuberculous process, external to the dura in my first case, has been the cause of the meningomyelitis, but it seems probable. If now a simple meningomyelitis may be produced by a process probably tuberculous external to the dura, what is there objectionable in the theory that it may also be produced by a tuberculous process external to the vertebræ?

Boettiger§ has attempted to show that the tuberculous and

*Spiller, International Med. Mag. 1897.

†Pfeiffer, Deutsche Zeitschrift für Nervenheilkunde, Vol. I.

‡Nageotte, Revue Neurologique, 1895.

§Marguliés, Neurologisches Centralblatt, 1896, p. 347.

‖Dejerine and Thomas, Comptes rendus de la Société de Biologie, 1896, p. 679.

¶Spiller, The Journal of the American Medical Association, April 9, 1898.

*Oppenheim, Lehrbuch der Nervenkrankheiten, p. 224.

†Welch and Flexner, The Johns Hopkins Hospital Bulletin, II, 107, 1891; III, 17, 1892.

‡Flexner, The Johns Hopkins Hospital Reports, VI, 1897.

§Boettiger, Archiv für Psychiatrie, Vol. XXVI, 1894.

the syphilitic meningomyelitis are the same in their histological appearances, and Raymond says that "the syphilitic meningomyelitis at its commencement has nothing specific but its cause; it has nothing specific so far as relates to the appearances under the microscope."* It therefore follows from this and other papers that the tuberculous meningomyelitis has nothing specific histologically at its commencement except the bacillus.

Virchow† teaches, if I understand him rightly, that in contusion and similar conditions with extravasation of blood, chemical products are formed which act as irritants with or without the presence of bacteria, and he compares these products with those formed by the micro-organisms. If this is true it may have some relation to the meningomyelitis in my first case.

I have been much interested in trying to find the nature of this round cell proliferation observed in these and other cases of meningomyelitis, and its final destiny. Raymond (*l. c.*) speaks in very positive terms, and Virchow (*l. c.*) in his paper on inflammation says that even yet the expression "small cell infiltration" is commonly used. I have been frequently struck by the expression "leucocytic infiltration," and have sought to find some authority for its use. It seems to be the opinion of some writers that unless we find multinuclear cells or cells with multilobular nuclei we have no right to speak of "leucocytic infiltration," and that we should regard the cells containing little protoplasm and large single and round nuclei as proliferations of connective tissue or its analogon, the neuroglia. But surely there are such cells as these within the blood.

Raymond (*l. c.*), in speaking more especially of syphilis, tells us that these round cells may undergo a retrograde change and disappear, or that they may form larger or smaller masses and undergo a gummatous change, or that they may form connective tissue and give rise to sclerosis.

Strümpell‡ takes a very decided stand in regard to the presence of meningomyelitis in Pott's disease. He says that all the changes in the spinal cord in spinal caries are only the necessary consequences of purely mechanical pressure. "At all events," he continues, "as we must state after numerous examinations made by us, in opposition to the prevailing view, no one has the slightest right to explain the paralysis occurring from spondylitis as the result of secondary myelitis." If preparations are made from the spinal cord, there are, according to Strümpell, no vascular changes to be found, no hyperæmia, no accumulations of cells about the vessels, and only occasionally small traumatic hæmorrhages. Frequently there are foci of degenerating nerve fibres, groups of swollen axis cylinders with partial or complete loss of their medullary sheaths, and in places spaces from which the nerve fibres have disappeared. In later stages there is proliferation of the neuroglia.

We can hardly be in doubt from this as to what Strümpell considers evidences of inflammation, for our views on this subject do not always harmonize.

Strümpell finds a supporter in Kraske (*l. c.*), who also says that the paralysis cannot be attributed to secondary inflammatory changes in the cord, and that this is equally true of the rare cases in which the cord is involved in the tuberculous inflammation, for this involvement occurs after the paralysis and toward the end of life. He acknowledges that the views regarding the relation of the paralysis to the tuberculous inflammation are still contradictory to one another.

Dinkler* reports a case in which two lesions were present in the spinal cord, one at the second and third thoracic segments, and one at the sixth, seventh and eighth thoracic segments. The lower lesion was evidently the older and showed proliferation of the glia, round cell infiltration, distension of vessels, etc. The upper lesion Dinkler regarded as the result of a dural tuberculosis, and he states that it was a typical compression lesion such as was described by Schmaus. Dinkler mentions, however, that at this upper level he noticed round cell infiltration in the pia and arachnoid. It seems to me, therefore, that both these lesions must be regarded as inflammatory. Dinkler states that tuberculosis of the lungs and vertebræ often causes mixed infection, and he thinks the lower lesion was possibly a metastatic process which had its origin in the pulmonary tuberculosis. It is difficult to see why the lower lesion should not be regarded as tuberculous, but be that as it may, it is evident that meningomyelitis may be caused either directly or indirectly by the tubercle bacillus, and even before paralysis appears, as in my first case.

Fürstner† observed intense round cell infiltration of the membranes and cord in a case of Pott's disease. He had operated on his patient, but there is no reason to think the cord was infected at the time of operation. It would not be difficult to quote other cases of Pott's disease in which meningomyelitis was observed.

In one of my cases there are large accumulations of round cells within the cord about the vessels, vascular dilatation and some swollen axis cylinders. These are distinct signs of inflammation, and indeed it seems to me after reading Virchow's recent address in Moscow that we should regard the swelling of the axis cylinders as a sign of parenchymatous inflammation. If we do so, we shall have difficulty in separating degeneration of nerve tissue from inflammation. These are Virchow's words: "I chose the name of parenchymatous inflammation for that process which, in the first place, produces swelling of the specific portions."

It is not easy, according to Bruns,‡ to determine the truly inflammatory nature of myelitis, and anatomically it is possible with certainty only in the very rare cases in which the producers of the inflammation (Entzündungserregern) have been shown to be present in the cord. By this I suppose he means the bacteria. All other histological findings which are regarded as characteristic of inflammation are found in cases of tumor and compression, cases which cannot truly be regarded as inflammatory. They are present also in thrombotic softening.

*Raymond, Leçon sur les maladies du système nerveux, deuxième série, p. 491.

†Virchow, Virchow's Archiv, Band 149, Folge XIV, Band IX, 1897.

‡Strümpell, Lehrbuch der spec. Path. u. Ther., Vol. III.

*Dinkler, Deutsche Zeitschrift für Nervenheilkunde, Vol. XI, Nos. 3 and 4.

†Fürstner, Archiv für Psychiatrie, XXVII.

‡Bruns, Allgemeine Zeitschrift für Psychiatrie, Vol. LIII, p. 614.

In contradiction to the statements of Strümpell, Noble Smith* informs us that the nerve symptoms in spinal caries are much more frequently the result of the inflammatory process extending to the cord or nerves than they are of pressure. This, however, does not seem to be the generally accepted view. I cannot follow Smith when he says that recovery occurring after symptoms of paralysis may indicate regeneration of pyramidal fibres. While regeneration frequently occurs in the peripheral nerves, and theoretically there is no reason why it should not occur within the cord, as a matter of fact the evidence of the latter is not satisfactory, as Leyden and Goldscheider state.

I shall merely touch upon the subject of operation in Pott's disease, as it hardly comes within the scope of this paper. Paralysis so frequently exists without degeneration of fibres that we can hardly be too cautious in suggesting surgical interference, at least by any of the older methods. It is not uncommon to find that the paralysis disappears even when it has existed for some time. It seems to be in these cases merely the expression of a functional change. Oppenheim† reports a case in which the paralysis disappeared after a duration of five or six years. Recently Calot's method has received great attention, although one writer states that its principle is as old as Hippocrates. This statement, however, can hardly detract from the honor due Calot. The time has been too short to judge fully of the efficacy of the method. The chief fear seems to be that the forcible reduction may arouse a quiescent process. In the first of my two cases there is a possibility that it might have increased the meningomyelitis, and in the second case it could have done little or no good, but in this case Calot would not have advised it.

Occasionally we hear of cases in which the method has not been successful and the patient has died of tuberculous meningitis after a few months. We cannot forget the hopes that were at one time raised by the suggestions of operation on the spinal vertebræ in Pott's disease, but the papers of Kraske (*l. c.*), Fürstner‡ and Dinkler§ are not encouraging, and Willard,‖ at a meeting of the New York Neurological Society, voiced the general opinion of those present when he spoke of the disappointment which has followed surgical interference in these cases by the older methods.

Discussion.

Dr. Barker.—There are many points in Dr. Spiller's report in common with a case which has recently been studied in the anatomical laboratory by J. Rosenheim. The latter has cut sections from many segments of the spinal cord of a case of Pott's disease, and although the results of the study have not yet been published, they are soon to appear. The pressure-lesion in Mr. Rosenheim's case was situated between the 8th cervical and the 4th thoracic nerves, some three segments of the spinal cord being extensively involved. Above the lesion there was marked degeneration of Gowers' tract and of the direct cerebellar tract as well as of the dorsal funiculi. Below the lesions there were the typical degenerations in the pyramidal tracts.

Dr. Spiller has been able to trace a degeneration in the comma tract for a distance of 4 cm. below the lesion; in Mr. Rosenheim's case it was possible to follow it through some three segments. We know now from the studies of Hoche, Mann and others that this tract is really a long tract extending throughout the whole thoracic region of the spinal cord. I did not understand from Dr. Spiller's paper whether or not he had found degenerations in the oval field of Flechsig in the lower portion of the cord. Mr. Rosenheim has been able to demonstrate degeneration in this area in his case, and there can be but little doubt from his findings and those in similar cases by Hoche that in some way or another certain fibres from the upper part of the cord are continuous with the oval field of Flechsig. It seems probable from Hoche's studies and from the researches of Bruce and Muir that there are two distinct descending endogenous tracts in the dorsal funiculi, one more ventrally placed corresponding to the "comma" tract and the "cornu-commissural fibres" of Marie; the other more dorsally placed and corresponding to somewhat scattered fibres in the upper portions of the cord, in the lower portions to more compact bundles, the septo-marginal tract of Bruce and Muir, the oval field of Flechsig, and further down the *triangle médian* of Gombault and Philippe. In order to bring these endogenous fibres of the dorsal funiculi into accord with corresponding fibres in the ventral and lateral funiculi I would suggest that we speak of the two tracts together under the name of the *fasciculus dorsalis proprius*, distinguishing a *pars ventralis* from a *pars dorsalis*.

I am glad that Dr. Spiller has referred to the views of von Bechterew and others regarding descending fibres in the region of the pyramidal tracts, which probably have their origin in centres below the pallium. There is much evidence in favor of the view that very numerous nerve fibres come down from the region of the inter-brain and the mid-brain to the medulla and to the spinal cord, fibres which throw the lower motor neurones under the influence of higher centres. Without such fibres it would be difficult to explain many of the facts of comparative anatomy and of ontogeny. The studies of Dr. Mellus show the importance of the substantia nigra as a way-station between the pallium and lower centres.

The changes referred to in the nucleus dorsalis of Clarke are of especial interest, and Dr. Spiller has brought further confirmation of the view now universally held that the fibres of the direct cerebellar tract represent the medullated axones of the cells in the nucleus dorsalis. Thus far no one, unless it be Laura, has actually demonstrated the connection of Clarke's nucleus with the fibres of the fasciculus cerebello spinalis. The embryological studies of Flechsig, however, and the results of experimental degeneration as investigated by Mott, taken together with evidence which has been afforded by the study of changes in the nucleus secondary to lesions of the tract (as in cerebrospinal meningitis), make it almost certain that the axones of the tract and the cells of the nucleus both represent constituent portions of the same set of neurones.

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* Smith, Spinal Caries, second edition.

† Oppenheim, Berliner klin. Wochenschrift, No. 47, 1896.

‡ Fürstner, Archiv für Psychiatrie, XXVII.

§ Dinkler, Deutsche Zeitschrift für Nervenheilkunde, Vol. XI, Nos. 3 and 4.

‖ Willard, Journal of Nervous and Mental Disease, April, 1897.

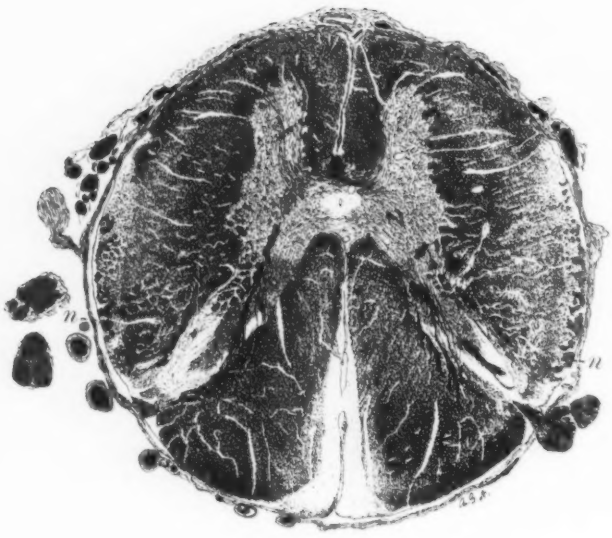

FIG. 1.

Section just below the pyramidal decussation. The columns of Goll are entirely degenerated, with the exception of a few fibres along their periphery, and do not extend to the posterior commissure. The columns of Burdach are slightly degenerated adjoining the columns of Goll. Normal fibres are found in the area of the direct cerebellar tracts (*nn*).

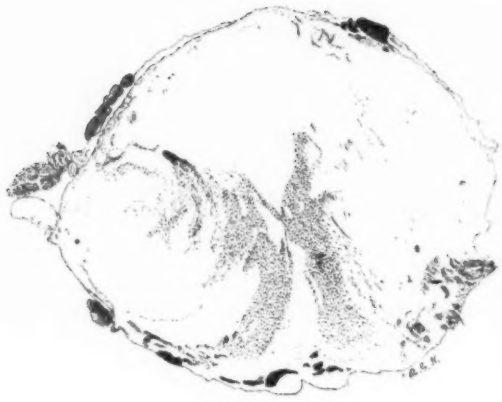

FIG. 3.

Section from the region of greatest compression, at the cervico-thoracic junction of the spinal column. The normal arrangement of the white and gray matter is entirely altered, and only a few normal fibres are present within the cord.

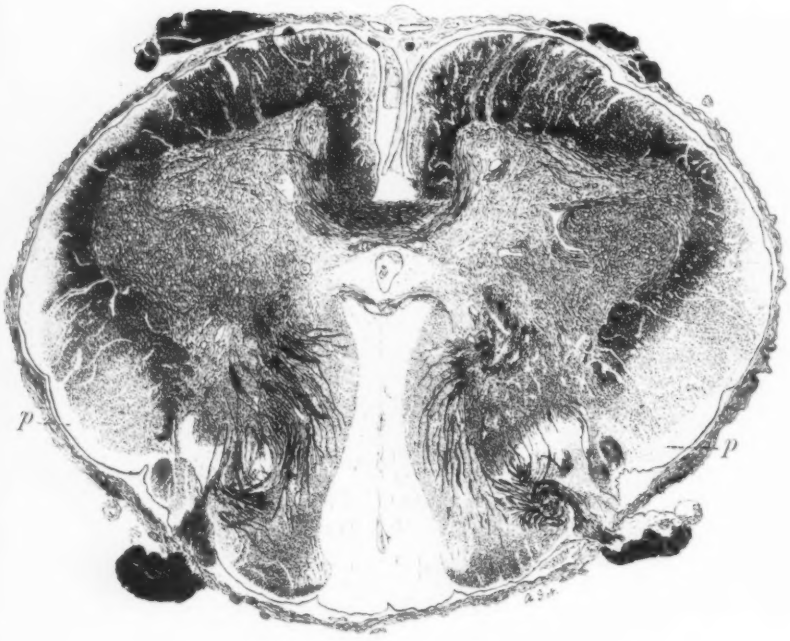

FIG. 2.

Section from the mid-cervical region. The direct cerebellar tracts (*pp*) and columns of Gowers are greatly degenerated. The crossed and direct pyramidal tracts are also much degenerated. The columns of Goll extend to the posterior commissure. The columns of Burdach are not entirely free from degeneration.

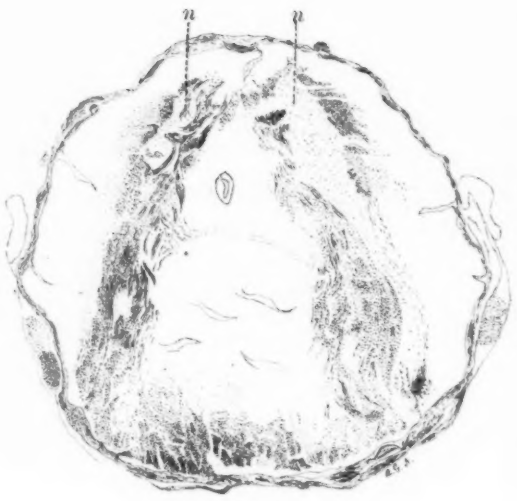

FIG. 4.

Section from the lower part of the compressed area. The anterior horns *nn* are indistinctly marked out by normal fibres in the adjoining columns. The greater portion of the section is entirely degenerated.

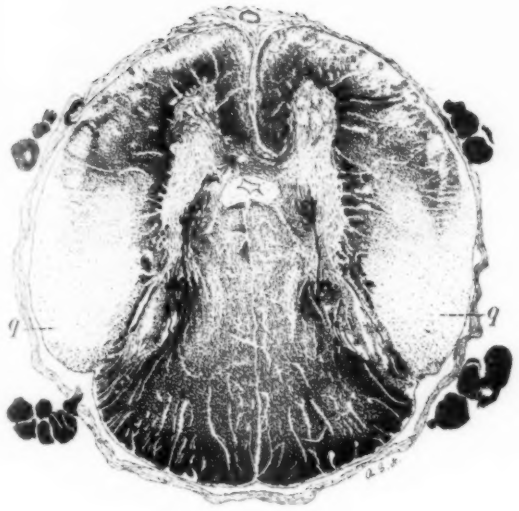

FIG. 5.

Section 3½ cm. below Fig. 3. The antero-lateral columns, including the direct cerebellar and Gowers' tracts (*qq*) and the periphery of the anterior columns, are greatly degenerated. The ventral portion of the posterior columns is also distinctly degenerated.

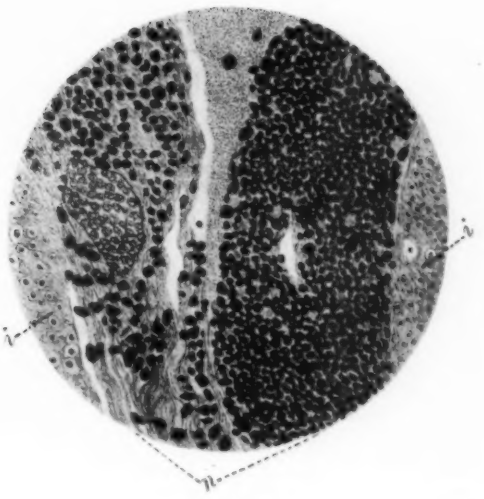

FIG. 7.

Section from the mid-cervical region in Case I, showing intense cellular infiltration in the posterior septum (*n*) near the posterior commissure. *ii* Right and left columns of Goll.

FIG. 6.

Section from the mid-lumbar region. The direct (*rr*) and crossed pyramidal tracts are degenerated.

Figures 1 to 6 inclusive are from Case II.

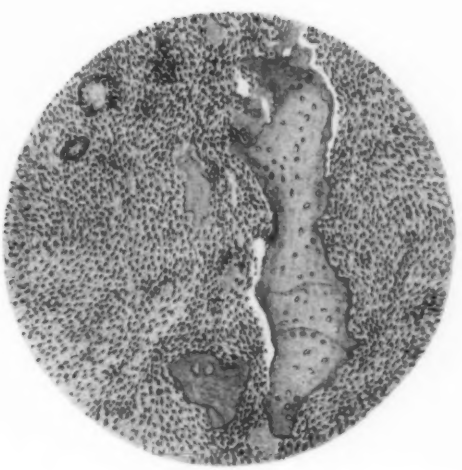

FIG. 8.

Osteoidmasses contained within the tuberculous exudate in the thoracic region (Case I). The majority of them are present in the outer zone of the exudate near the bony canal and only slightly removed from the intervertebral discs which show irregularities and are becoming clarified.

Dr. FLEXNER.—Dr. Spiller's paper is an embarrassment of riches. There are two or three points only which the limited time will permit me to refer to. The first concerns the relation of degeneration in the nerve-roots and peripheral spinal nerves to changes in the motor cells of the anterior horns. I was surprised at the slight changes observed in the cells notwithstanding the extensive degenerations of the nerves. It is, of course, unnecessary to remind Dr. Spiller, or this audience, of the experimental and other work of Von Gudden, Friedlander, Grigoriew and Nissl, which has shown that the nerve cells suffer severely following injury to and removal of the peripheral nerves.

Dr. Spiller's remarks on this topic have raised the question of what characters stamp an inflammation as specific, that is, in this instance, as tuberculous. We have come to recognize in the micro-organisms of the specific diseases a capacity to produce definite histological structures which can be at once recognized as due to that cause—so, for example, the miliary tubercle—and at the same time, to give rise to other changes of a simple and non-specific inflammatory type. The thickening of the framework in the lung in tuberculosis is one example of such an action, and many other fibroid and degenerative processes in the body have the same origin. An intermediate sort of lesion is found in the diffuse tuberculous tissue in which even giant cells may be wanting and blood-vessels present, and whose specific characters are given through the presence of tubercle bacilli and the degenerations which it tends to undergo. The crucial test, of course, is the finding of the tubercle bacillus, and in many chronic conditions this is a laborious undertaking.

It is interesting to have Dr. Spiller bring up again the Virchow conception of parenchymatous inflammation. Since the days of Cohnheim, pathologists have demanded something more than a mere degenerative lesion before stamping the process "inflammation," and they have attempted, although it must be confessed not always with success, to mark off more sharply simple degenerative from actual inflammatory changes.

Dr. SPILLER.—It is well known, as Dr. Flexner states, that the cells of the anterior horns of the spinal cord are affected by degenerative changes in the anterior roots. It is much to be regretted that the spinal cord in my first case was hardened in Müller's fluid and that the application of the Nissl stain was impossible. In the thoracic region the motor cells were distinctly altered. Could the Nissl stain have been employed, the cells of the mid-cervical region might also have been found degenerated. I have not intended to deny the existence of cellular lesions in the latter portion of the cord visible by Nissl's method, but I place very little value on studies of cells stained by carmine alone, unless the changes are of an intense degree.

I have been unable to stain the tubercle bacillus in this tissue hardened in Müller's fluid, but Dr. Abbott and Dr. Flexner tell me that they know the bacillus has been found under similar conditions. As Dr. Flexner puts it, "it is a labor of love."

It is impossible to assert that the myelitis in my first case has been caused by the tubercle bacillus, though I have found no other cause. It is, however, a very important fact that myelitis of considerable intensity, with polynuclear and mononuclear cellular infiltration, may occur in Pott's disease, and it is possible that some of the symptoms of this disease may at times be due to the myelitis and not entirely to the compression.

I should like to emphasize the statement that the degeneration of the posterior columns in my second case was not confined to Schultze's comma zones, but was much more extensive. This diffuse form of descending degeneration in the posterior columns of the cord has rarely been reported, and is entirely different from the degeneration frequently observed in Schultze's comma zones, inasmuch as it is not systemic.

Note on the osteoid tissue found in the tubercular exudate in the thoracic region of the cord.—Dr. FLEXNER.

There is contained amid the typical tuberculous exudate, outside the dura, scattered masses of osteoid tissue. These are of irregular form and shape. They consist of a ground substance which is homogeneous or faintly granular or fibrillated, and contain irregular nuclei resembling, in part, bone corpuscles. For the most part the masses are non-calcified. But now and then calcification can be seen to be going on, and in such cases the masses take a blue hæmatoxylin stain. The majority of the flakes are in the outer zone of the exudate nearest the bony canal; and the cartilage of the intervertebral discs (?) shows slight irregularity, and in places is undergoing calcification. It is therefore not improbable that serial sections might have shown the osteoid masses to have originated from the intervertebral cartilages.

A CASE OF OSTEITIS DEFORMANS.*

BY WM. T. WATSON, M. D., *of Baltimore.*

In 1876 Sir James Paget reported to the Medical and Chirurgical Society of London, five cases of a previously undescribed disease to which he gave the name "Osteitis Deformans." He described one case in great detail and gave reports of both microscopical and chemical examinations of the bone. Although a good many cases have since been reported, about sixty in all, nothing very material has been added to the description of the disease as first given by Paget. He gave as the chief characteristics of the disease the following:

It begins in middle age, or later; is very slow in progress; may continue for many years without influence on the general health, and may give no other troubles than those which are due to the changes of shape, size and direction of the diseased bone. Even

*Read before the Johns Hopkins Hospital Medical Society, February 7, 1898.

when the skull is hugely thickened and all its bones exceedingly altered in structure the mind remains unaffected.

The disease affects most frequently the long bones of the lower extremities and the skull, and is usually symmetrical. The bones enlarge and soften, and those bearing weight yield and become unnaturally curved and misshapen. The spine, whether by yielding to the weight of the overgrown skull, or by change in its own structures, may sink and seem to shorten, with greatly increased dorsal and lumbar curves; the pelvis may become wide; the necks of the femora may become nearly horizontal, but the limbs, however misshapen, remain strong and fit to support the trunk.

In its earlier periods, and sometimes through all its course, the disease is attended with pains in the affected bones, pains widely various in severity and variously described as rheumatic, gouty or neuralgic, not especially nocturnal or periodical. It is not attended with fever. No characteristic conditions of urine or feces have been found in it. It is not associated with syphilis or any other known constitutional disease, unless it be cancer.

The bones examined after death show the consequences of an inflammation affecting, in the skull the whole thickness, in the long bones chiefly the compact structure of their walls, and not only the walls of their shafts, but, in a very characteristic manner, those of their articular surfaces.

In 1890, fourteen years later, after Paget had seen 23 cases of the disease, he made the following statement:

1. The preponderance of males among the patients affected with this disease is confirmed.

2. The most frequent ages at which the disease was first observed were between 40 and 50.

3. The frequency of cancer or sarcoma occurring in those affected with osteitis is confirmed. Of eight cases traced to the end, five died with cancer or sarcoma. This fact, confirmed as I believe it is by the observations of others, is decisive as to an intimate relation between osteitis and the formation of malignant tumors. I do not venture to guess what that relation is.

4. It may be only by chance coincidence, but it seems worth mentioning that in 23 cases, 4, after long continuance of the osteitis, became blind—1 with choroiditis, 3 with retinal hæmorrhages.

5. I have tried in vain to trace any inherited tendencies to the disease. Many have had gouty ancestors, but I do not think more than any other equal number of persons in the same rank in life.

6. The most frequent seats of the osteitis are the tibiæ, femora, clavicles, spine, and vault of the skull. The posterior and regularly median curvature of the spine is always well marked, the pelvis often broad. I have never seen any evidence of the disease in the bones of the face, hands or feet. In this respect the contrast with the acromegaly of Marie has seemed complete.

The morbid anatomy, as given by Paget, is as follows:

Periosteum not visibly changed. The outer surface of the walls of the bones irregularly and finely nodular, as with external deposits or outgrowths of bone, deeply grooved with channels for the periosteal blood-vessels, finely but visibly perforated in every part for the transmission of the enlarged small blood-vessels. Everything seemed to indicate a greatly increased quantity of blood in the vessels of the bone.

The medullary structures appeared to the naked eye as little changed as the periosteum. . . . The medullary spaces were not encroached upon.

The compact substance of the bones was in every part increased in thickness. . . . In the greater part of the walls of the shafts of the bones the whole construction of the bone was altered into a hard, porous or finely reticulate substance like very fine coral. In some places there were small, ill-defined patches of pale, dense and hard bone, looking as solid as a brick.

In the compact covering of the articular ends of the long bones . . . the increase of thickness was due to encroachment on the cancellous texture, as if by filling its spaces with compact porous new-formed bone.

The microscopical appearance as given by Mr. Butlin is as follows:

The number of Haversian systems and canals in any given section would seem to be much diminished. The space between the Haversian canals was occupied by ordinary bone substance, containing numerous lacunæ and canaliculi. The Haversian canals were enormously widened, many of them were confluent, and thus the appearance of a number of communicating medullary spaces was obtained; an appearance that was rendered still more striking by the presence in the canals of a large quantity of ill-developed tissue in addition to the blood-vessels.

The contents of the Haversian canals were seen to consist generally of a homogeneous or granular basis, containing cells of round or oval form, about the size and having much the appearance of leucocytes. Larger nucleated cells were also present, and fibres or fibro-cells sometimes in considerable quantity. Myeloid cells were occasionally observed, but they were not plentiful. Fat also existed in many of the larger spaces, especially in the skull. The vessels were unusually small compared with the channels in which they ran; indeed, they did not seem to be larger than those of normal bones.

The walls of some of the canals were lined by a single layer of osteoblasts—a condition precisely similar to that observed in a normal ossification of the bone in membrane.

The presence of new bone was most evident in the periosteum of the tibia, external to the ordinary compact layer of the shaft. This external layer was of course but thin, and was much softer and less developed than the cortex of the bone from which it sprung. It evidently was not nearly sufficient to account for the great increase in the diameter of the tibia. There was no similar recent formation of bone on the outskirts of the medullary canal.

The number of lamellæ surrounding the Haversian canals was no larger than in normal bone, whilst the arrangement of the intervening space was most complex and totally different from that of healthy bone. Lacunæ and canaliculi throughout the sections did not strikingly differ from those of ordinary bone.

As to the nature of the disease, Paget, Butlin, Clutton, Eve, Silcock and others believe it to be a chronic inflammation of bone, but Goodhart, Lunn and others do not deem that its inflammatory nature has been proven.

Lunn, who reported 4 cases in 1885, while admitting that chronic inflammation might have some share in the process, thought that it would not altogether account for the changes found after death. His conclusions were that osteitis deformans consists of—

1. A constitutional disease, producing atrophy and absorption of a large part of the osseous system.
2. Consequent weakening of the bones so that they yield when exposed to strain.
3. Compensatory strengthening by the growth of what may be looked upon as a variety of callous.
4. The occasional formation of definite tumors.
5. A fatal cachexia.

Commenting upon these views, Silcock, in 1885, said:

It is difficult to imagine how a process can primarily be one of atrophy and absorption when the first recognizable sign of the disease is the thickening and enlargement of the bone. Nor can the superadded bone in this case be regarded in the light of "compensatory strengthening" of the curves, or of a buttress-like forma-

FIG. 1.

Skiagraph of left knee joint. Tibia greatly enlarged. Fibula apparently normal.

FIG. 2.

R. at 36 years of age.
Height 5 ft. 11¾ inches.

FIG. 3.

R. at 62 years of age.
Height 5 ft. 2½ inches.

FIG. 4.

Side view, showing bowing of back and lower extremities.

FIG. 5.

Head view, showing enlargement of cranium, the face bones remaining normal.

FIG. 6.

Skiagraph of left tibia, showing marked anterior curvature, and great thickening. Dark and light areas probably correspond to areas of condensation and rarefaction.

tion, since the mass of it is deposited on the convexity of the curve and not in the concavity. Again, the external thickening of the bones of the cranium is wholly inexplicable on the theory enunciated. As held by Paget and Butlin, the essential features of the osseous lesions of the disease are indistinguishable from, if not highly characteristic of, inflammation.

Concerning the etiology of osteitis deformans absolutely nothing is known.

It is more frequently seen in England than elsewhere, and is more common in London than in other parts of England. This fact led Johnathan Hutchinson to conclude that the malady was probably connected with gout, but this view has not been accepted by others.

Diagnosis: The diseases with which it might possibly be confounded are rickets and osteomalacia. In rickets the bones are too short and not too long, too small, not too large; and their curvatures are not like those of osteitis.

In osteomalacia the walls of the bones become exceedingly thin, and when they yield it is not with regular curving, but with angular bending or breaking.

The course of the disease is very chronic. When death ensues it is from some coincident disease which has been aggravated by the condition of the bones only in so far as they may have diminished the range of breathing and the general muscular activity.

Six cases of this disease have been reported in America, the first by McPhedran in Toronto in 1885, the second by Gibney in New York in 1890, the third by Mackensie in Toronto in 1891, the fourth and fifth cases by Taylor in New York, 1892, and the sixth by Herwisch in Philadelphia in 1896.

The present case is then the seventh to be reported in America and is more typical than any of the others.

I had hoped to be able to bring the case before you to-night, but have been disappointed. I have, however, some photographs which will in some measure make up for his absence.

R., aged 62. Family history unusually good. His father was a French Canadian, born near Montreal, who "never had a day's sickness," and died of congestion of the brain at the age of 79. His father's brother, at the age of 100, was killed while walking on a railroad track. His mother was born in New Jersey and died on her 90th birthday of old age. He has two brothers living at the ages of 72 and 75. No relative ever died of cancer.

Personal history. He was never in bed a day from any illness. A slight attack of measles in childhood and a carbuncle ten years ago were his only ailments. He has always led a very active life. He conducted a successful business from 1860 until 1886, and did not then retire on account of physical or mental disability. Every year since he was a boy he has indulged in fishing, duck shooting, sailing and outdoor sports. Up to the age of 42 he was strong and active, "as straight as an arrow," and five feet eleven and three quarter inches in height.

The present malady began about 25 years ago, when the skin over the anterior portion of the upper half of the left leg became inflamed, the inflammation gradually spreading to the ankle. Later on an inflammation appeared on the corresponding portion of the right leg. This lasted four or five months and then subsided, leaving behind some large pigmented areas.

About twenty years ago he began to have pains in the bones and calves of his legs. The calf muscle would be drawn into bunches. These pains have persisted more or less ever since, usually worse at night. At the onset of these pains he noticed for the first time that his legs were bending and his height was diminishing. This bending of the legs has steadily advanced and is still progressing.

About fifteen years ago the increased size of his head began to attract attention. This increase, the patient is confident, began 35 years ago, when at the age of 27 he had to increase the size of his hat from a No. 7 to a 7½. At intervals of four to five years he has had to take a hat a size larger, until now he wears a No. 8. This indicates a total change in circumference of $3\frac{1}{16}$ inches. There has been no evident increase in the size of the head for three or four years past. He has never had pain or discomfort of any kind in his head.

Ten years ago his back commenced to bow and the shape of his chest to change, becoming flatter in front. These changes are still progressing. His height was formerly five feet eleven and three quarter inches. In July, 1897, it was five feet three inches. At the present time it is five feet two and one-half inches. Total loss in height nine and one quarter inches. This loss of height, due to bowing of the back and lower extremities, is rapidly progressing.

The general health of the patient has continued very good. While his gait is awkward it is steady, and his only complaint is of the pains in his legs and thighs, which are not so annoying as formerly. His intellect is unimpaired.

In the fall of 1896 he went on a hunting trip. When attempting to take aim he found to his surprise that he could not see with his right eye.

Present condition. In July, 1897, I took R. to Dr. Osler, who made the diagnosis and dictated the following note:

"Head fairly symmetrical, looks large; the most marked prominences are just over the temporal muscle at the squamo-parietal junction. Above this there is a distinct groove like flattening, and then a marked prominence on either side of the parietal suture. The posterior parts of the parietal bone and the occipital bone are uniform and symmetrical.

No apparent enlarging of the bones of the face; no enlarging of the jaws or of the zygoma; in fact the face looks small in proportion to the size of the head. Teeth are bad; nearly all gone. No enlargement of maxillary process.

Body: No enlargement of cervical vertebræ. A most remarkable bowing of the dorsal spine. The lordosis is of the most extreme grade. There is no special prominence of any of the vertebræ. The ribs do not appear to be enlarged. The chest, from the front, is singularly box-shaped, a perfectly quadrilateral thorax. There is a little scoliosis, the curve being towards the left.

No enlargement of the clavicle or shoulder-blades. No enlargement of the bones of the arm or of the hand. No clubbing of the fingers. Dupuytren's contraction in both hands.

The pelvis is not enlarged, crests of the ilia feel normal.

Legs are remarkably bowed. With the heels together, from

the inner side of one knee-pan to the other is 23 cm. From the crest of one tibia to the other is 26 cm. The thigh bones do not seem enlarged. The tibiæ present the most remarkable deformity. They are both extremely curved anteriorly, enormously enlarged; a condition of diffuse hyperostosis. The left leg is larger than the right. Measurement of the most prominent part of the calf: left, 37 cm.; right, 35.5 cm. The bones are smooth and uniform, except on the anterior margin, where both are a little rough. The fibulæ feel a little enlarged at the upper end, but do not seem to be involved to the same extent. On the anterior surface of both legs and over the outer maleoli there are old pigmented changes in the skin, which is rough and hard. Both inner condyles of the femur look enlarged. Measurements over the knee joint: right, 39.5 cm.; left, 38 cm. Height five feet three inches."

Dr. Reik has recently examined his eyes and reports as follows:

Mr. R. has a high grade of myopia, with large posterior staphyloma and extensive choroidial changes in each eye. In the right eye there is in addition a central lens opacity and consequently vision is practically nil. Vision in the left eye is $\frac{10}{30}$ with a —12 Ds.; with a —8 Ds. he can read Jaeger No. 1.

Discussion.

Dr. Cone.—It is interesting in the bibliography of this case to bring in the work of Von Recklinghausen. He mentions cases of osteitis deformans in which there was a development of fibroma and of sarcoma, and mentions also that cysts frequently form in these cases, and he describes them very fully. The walls are fibrous, contain a spongy network of bone, and outside of this is fatty marrow. He mentions that the seat of these changes is the spots where the bone is under most statical pressure. As to the inflammatory origin of the disease, there is one case cited by Gruber in which, following erysipelas, there was this hyperostosis and a condition resembling elephantiasis.

Dr. Watson.—In reply to Dr. Osler I would say that in Paget's experience the cranial bones were frequently affected. In four of the six American cases there was enlargement of the head. In Mackensie's case, aside from some spinal curvature, a very much enlarged cranium was the sole lesion. In Herwisch's case, in addition to an enlarged cranium there was some thickening and curving of the femora and left tibia and some thickening of the crests of the ilia. In the case of Dr. Gibney the head was increased in size and the legs very much bowed.

In one of Dr. Taylor's cases there was a very large head, considerable bowing of the spine, some enlargement of the pelvis and enlargement and bowing of the right femur. In his second case there was no head enlargement, the sole lesions consisting of enlargement and bowing of the right femur and some lateral spinal curvature. In McPhedran's case the only bones involved were the right tibia and femur.

The case reported to-night corresponds more closely to Paget's description than any of the American cases, although one of Dr. Taylor's cases is almost as typical.

The statement made by Paget that there is a preponderance of males among the patients affected with this disease seems to be contradicted by later statistics, for of 43 cases analyzed by Thieberge in 1890, 21 were men and 22 were women.

THE RISE OF THE THEORY OF ELECTROLYTIC DISSOCIATION, AND A FEW OF ITS APPLICATIONS IN CHEMISTRY, PHYSICS, AND BIOLOGY.*

By Harry C. Jones, Ph. D., *Instructor in Physical Chemistry, Johns Hopkins University.*

It is doubtless unusual for this Society to be confronted with a subject which is apparently so widely removed from medicine as that of physical chemistry. But since certain comparatively recent developments have made it probable that the latter is destined to exert some influence upon the former, I have been kindly asked by your President to discuss that side of physical chemistry which has already been brought in touch with certain biological problems. I shall therefore give a very brief account of the origin and development of the theory of electrolytic dissociation, which is one of the keystones to the whole science of physical chemistry.

The botanist, Pfeffer, carried out a quantitative investigation of the osmotic pressure which solutions of both non-electrolytes and electrolytes exert against the pure solvent. His work is so well known that a mere reference to it is nearly sufficient. The artificial membranes which he devised, by depositing some finely divided precipitate, such as copper ferrocyanide, in the walls of fine-grained porcelain, were semipermeable, *i. e.* they allowed the solvent to pass through them, but prevented the dissolved substance from doing so. With such membranes he was enabled, for the first time, to make a careful quantitative study of the amount of osmotic pressure which different substances exert.

The results of Pfeffer were examined by Van't Hoff, who pointed out that they led to the following interesting and important generalizations:

I. The osmotic pressure of solutions of non-electrolytes is proportional to the concentration.

II. The temperature coefficient of osmotic pressure is very nearly $\frac{1}{273}$ of the osmotic pressure, for every degree Centigrade.

III. The osmotic pressure of a solution is *exactly equal to the gas pressure* which the dissolved substance would exert, if it were present as a gas, in a space equal to that occupied by the solution. A molecule exerts the same osmotic pressure as it would exert gas pressure under the same conditions of temperature.

*Read before the Johns Hopkins Hospital Medical Society, March 7, 1898.

These three laws of osmotic pressure will be recognized, at once, to be strictly analogous to the three laws of gases—that of Boyle, that of Gay-Lussac, and that of Avogadro.

Van't Hoff further pointed out that the electrolytes—strong acids, and bases, and the salts—present exceptions, and exercise a greater osmotic pressure, for equivalent concentration, than the non-electrolytes.

The explanation of this difference was offered by Arrhenius. He studied the depression of the freezing-point of water produced by both electrolytes and non-electrolytes, and found that the former was always greater than the latter. He took into account, also, the property of solutions of electrolytes to conduct the current, and pointed out a quantitative relation between the conductivity of such solutions and the depression of the freezing-point of the solvent produced by the dissolved electrolyte. He showed, thus, that solutions of those substances which give abnormally large osmotic pressure, give abnormally great depression of the freezing-point of the solvent, and conduct the current.

It had already been shown by Raoult, that the depression of the freezing-point of a solvent by any dissolved substance, depended upon the relation between the number of parts of the dissolved substance and of the solvent. It seemed, then, that in the case of electrolytes there were more parts of the electrolyte present than could be accounted for on the assumption that the substance was present in the solution in the simplest molecular condition. To account for such facts as these, Arrhenius proposed the theory which has become so well known as the theory of electrolytic dissociation. When an electrolyte is dissolved in a solvent like water, the molecules break down, not into atoms, but into ions, which are atoms, or groups of atoms, charged with electricity. The amount of such dissociation is dependent upon the concentration of the solution. The more dilute the solution, the greater the dissociation of the molecules into ions, and at about one one-thousandth normal, the dissociation of all the strong acids, and bases, and most of the salts, is complete. This means that there are no molecules of the electrolyte present, but only the ions into which the molecules have dissociated.

This suggestion, it must be said, is not entirely new with Arrhenius, it is closely related to certain views held by Grotthuss, Williamson and Clausius. But the broad application of the theory to these newly discovered facts, together with quantitative methods for measuring the amount of the dissociation in a given case, we owe to Arrhenius.

Given the theory, the all-important question remains, is it true? The time at my disposal will not permit me to discuss many of the lines of evidence which bear upon the theory of electrolytic dissociation. It is so far-reaching in its significance, so fundamental in its bearing, that any physical or chemical property of solutions can reasonably be summoned to furnish evidence as to its validity. I will refer very briefly to a few points which bear directly upon the theory in hand. If dilute aqueous solutions of electrolytes contain only ions, and no molecules, then it is clear that all the properties of such solutions must be the properties of ions, and not of molecules, since there are no molecules present. But since a molecule always dissociates into at least two ions—a cation, which is charged positively, and an anion, which is charged negatively—the properties of completely dissociated solutions must be a function of two constants, the one depending upon the cation and the other upon the anion. If we study the physical properties of such solutions, such as their specific gravity, power to refract light, power to rotate the plane of polarization of light, color, etc., we find that they are the sum of a constant for the cation and a constant for the anion.

If we turn to the property of completely dissociated solutions to conduct the current, we find here again the same additive condition. The conductivity of these solutions is the sum of two constants, which is the well known law of Kohlrausch, usually expressed as the law of the independent migration velocities of the ions.

A quantitative test of the theory may be made by a study of the osmotic pressure of solutions of electrolytes. It will be remembered that the generalizations of Van't Hoff were reached through a study of Pfeffer's measurements of the absolute osmotic pressure exerted by non-electrolytes. Pfeffer found also that electrolytes exert a greater osmotic pressure than non-electrolytes. De Vries, using the plasmolytic, or living cell method, which gives only relative osmotic pressures, found, also, that electrolytes exert a greater osmotic pressure than non-electrolytes. This excess in the osmotic pressure of non-electrolytes is, in terms of the theory, due to a dissociation of the molecules into ions. De Vries showed that solutions of undissociated substances, containing the same number of molecules in a given volume, exerted the same osmotic pressure. Such solutions were terms *isohydric*. The same applies to solutions of electrolytes, with this difference, that at moderate dilutions we have to deal with the sum of the molecules and the ions present. De Vries was able by his method to determine the concentrations of solutions of electrolytes which are isohydric with one another. When these concentrations were represented in molecular quantities their reciprocal values were termed *isotonic coefficients*.

The dissociation of electrolytes can be calculated from the measurements of the osmotic pressure of solutions made by De Vries, and also from the measurements of the conductivity of the same solutions, and these two sets of values should agree with one another, if the theory of electrolytic dissociation is true. Below are given the amounts of the dissociation of a few substances, calculated for a given dilution, from osmotic pressure and from conductivity:

Substance.	Dissociation from Osmotic Pressure.	Dissociation from Conductivity.
KNO_3	69%	80%
$NaNO_3$	69	73
KCl	69	84
NaCl	71	82
$(COOK)_2$	61	66
K_2SO_4	60	67

Considering the large error involved in the osmotic pressure method, the agreement is probably within the error of experiment.

It was early found that the power of electrolytes to lower the vapor-tension, or to lower the freezing-point of the solvent in which they are dissolved, is greater than that of non-electrolytes. Either of these properties of solutions of electrolytes can be used to measure their dissociation. Since the method of measuring the freezing-points of solvents and solutions has been worked out far more accurately than the method of determining their boiling-points, the former is to be preferred as a method for measuring dissociation. I will give some results of the dissociation of electrolytes as calculated from my own measurements of the freezing-point depression of solvents, produced by them, and compare these with the dissociation of the same dilutions of the same electrolytes as calculated from Kohlrausch's conductivity work.

Substance.	Concentration. Gram-molecular normal.	Dissociation from Conductivity.	Dissociation from Freezing-point Lowering.
NaCl	0.001	98.0%	98.4%
"	0.01	93.5	90.7
"	0.1	84.1	83.5
KCl	0.001	98.0	101.0
"	0.01	94.2	90.7
"	0.1	86.0	83.4
H_2SO_4	0.003	89.8	86.0
"	0.005	85.4	83.8
"	0.05	62.3	60.7
HCl	0.002	100.0	98.4
"	0.01	98.9	95.8
"	0.1	93.9	88.6
HNO_3	0.002	100.0	98.4
"	0.01	98.5	96.8
"	0.1	93.5	87.8
KOH	0.002	100.0	98.4
"	0.01	99.2	93.7
"	0.1	92.8	83.1

These are but a few results taken from a large number, involving all classes of electrolytes—acids, bases, and salts. The agreement is so striking that comment is superfluous.

Another line of evidence is to be sought in the study of mixtures of salt solutions. In terms of our theory, a dilute solution of potassium chloride contains only potassium ions and chlorine ions, and, similarly, a dilute solution of sodium bromide contains only sodium ions and bromine ions. These facts would be expressed thus:

$$KCl = \dot{K} + \bar{Cl}$$

$$NaBr = \dot{Na} + \bar{Br}$$

A mixture of these solutions would contain, then, potassium, sodium, chlorine, and bromine ions; and all the properties of this mixture would be a function of the properties of these four ions, there being no molecules present. If, on the other hand, we started with potassium bromide and sodium chloride, and mix their dilute solutions, we would have exactly the same ions present, and the properties of the second mixture should be, for the same concentration, exactly the same as the first, and such is the case.

But if we should mix solutions of substances which are undissociated, such as methyl chloride and ethyl bromide, we ought to obtain a mixture with properties which are different from a mixture of methyl bromide and ethyl chloride, because we have here to deal only with molecules, which would be different in the two cases. And here again the facts agree perfectly with the theory. A mixture of methyl chloride and ethyl bromide has properties which are different from a mixture of methyl bromide and ethyl chloride.

Would that time permitted to take up an adequate number of the many lines of evidence which point to the theory of electrolytic dissociation in solution in water, and, to a less extent in many other solvents, but it does not.

I believe that when all the evidence at hand is taken into account, it points so conclusively to the general truth of the theory of electrolytic dissociation that we can accept it with the same degree of confidence as we do the law of Avogadro or many of the so-called laws of nature. And it may be said that the theory is now generally accepted by those who have impartially examined the evidence which is available.

If the theory be true, the question which next arises is, what is its scientific value? Has it been helpful in correlating facts which have hitherto appeared to be unconnected? If so, its value is apparent. Or does it suggest, or point out new lines of experimental investigation? If it does, its value is unquestioned. If it should assist in both of these directions, so much the greater is its worth. I can take up only a few examples. Take the well known reaction of the neutralization of acids and bases. In terms of the theory of electrolytic dissociation, a dilute aqueous solution of a strongly dissociated electrolyte contains no molecules, only ions. A solution of a base contains the hydroxyl anion, and a cation whose nature depends upon the base used. A solution of an acid contains the hydrogen cation, and an anion whose nature depends upon the acid chosen. Similarly, a solution of a salt is but a solution of anions and cations. To take as a concrete example, hydrochloric acid and sodium hydroxide, the reaction would be represented thus:

$$\bar{Cl} + \dot{H} + \bar{OH} + \dot{Na} = \bar{Cl} + \dot{Na} + H_2O,$$

or in general:

$$\bar{A} + \dot{H} + \bar{OH} + \dot{C} = \bar{A} + \dot{C} + H_2O.$$

The anion of the acid and the cation of the base remain unchanged in the process of neutralization, which consists only in the formation of water. If this is true, then the process of neutralization of a given acid by a given base, is the same as the neutralization of any other acid by any other base.

This can be tested directly by experiment. The heat liberated in the neutralization of an equivalent of a completely dissociated acid by an equivalent of a completely dissociated base, being always the heat of formation of the same amount of water from the ions $\dot{H}$ and $\bar{OH}$, must be a constant, independent of the nature of the acid or of the nature of the base. The following results show that this is true:

	HCl. HBr. HI.	HNO_3.	CH_3COOH.	HCOOH.
NaOH	13.7 Cal.	13.7 Cal.	13.3 Cal.	13.4 Cal.
KOH	13.7	13.8	13.3	13.4
$\frac{1}{2}Ca(OH)_2$	14.0	13.9	13.4	13.5
$\frac{1}{2}Ba(OH)_2$	13.8	13.9	13.4	13.5
$\frac{1}{2}Sr(OH)_2$	14.1	13.9	13.3	13.5

The agreement between the heats of neutralization is striking, in consideration of the necessary errors involved in thermo-chemical measurements.

The theory of electrolytic dissociation thus brings together all the processes of neutralization of acids by bases, and refers them to a common cause, the union of the hydrogen and hydroxyl ions to form water.

It may be stated that it has been shown by no less than a half-dozen separate pieces of work, that hydrogen and hydroxyl ions cannot exist in the presence of one another, in any appreciable quantity, uncombined; or, in a word, water is undissociated.

Another example may be taken from chemistry.

If the properties of solutions of electrolytes are properties of the ions, then what relation exists between the chemical activity of solutions and their dissociation? The dissociation of substances must be determined, and also their power to effect chemical reaction, and the results of these two measurements must then be compared. A few of the many results available will suffice to bring out the relation. In column I are given the dissociations of acids referred to hydrochloric acid as 100; in II, the velocities with which they effect the catalysis of methyl acetate; in III, the velocities with which they invert cane sugar.

	I.	II.	III.
HCl	100	100	100
H_2SO_4	65.1	73.9	73.2
HCOOH	1.68	1.31	1.53
CH_3COOH	0.42	0.34	0.40
$CH_2ClCOOH$	4.90	4.30	4.84
$CHCl_2COOH$	25.3	23.0	27.1
CCl_3COOH	62.3	68.2	75.4
$(COOH)_2$	19.7	17.6	18.6
$CH_2(COOH)_2$	3.1	2.87	3.08
$C_2H_4(COOH)_2$	0.58	0.50	0.55

The agreement is as satisfactory as the conditions would allow us to expect.

The strength of acids is thus directly proportional to their dissociation.

We then naturally look for a common cause of that property which we describe as *acid*, in compounds such as those given in the last table, and this is easily found. All of these compounds dissociate into a hydrogen cation ($\dot{H}$) and an anion, whose nature depends upon the compound in question, varying with every acid. Wherever we have hydrogen ions we have the acid property, and the strength of any acid depends only upon the number of hydrogen ions present.

The same applies to hydroxyl bases, where their strength depends upon the number of hydroxyl anions ($\bar{O}H$) present.

The direct quantitative relation between chemical activity and dissociation has now been so frequently established that we often use dissociation to measure chemical activity, and also chemical activity to measure the amount of dissociation.

And this raises the question as to whether chemical activity is due solely to ions. Are molecules incapable of reacting with one another? It would be going too far, in the light of our present knowledge, to maintain this. There are substances known which apparently do not conduct at all (are completely undissociated), and yet react chemically. There are cases known of dry solids, which we suppose contain only molecules, reacting with one another. We have well characterized chemical compounds formed by the union of two parts of apparently the same general electrical character: thus phosphorus and chlorine, chlorine and bromine, chlorine and iodine, etc. Yet chemical reactions in which acids and bases are involved are now known to be reactions involving only ions, molecules as such not coming into play. And indeed the number of reactions which are known to be purely ionic, is very great, including the majority of the cases with which we have to deal in chemistry.

The application of the theory of electrolytic dissociation is by no means limited to chemical phenomena. It touches with equal success, certain sides of physics. With its aid we are now able to calculate the electromotive force of many forms of primary cells, knowing the concentration of the solutions of electrolytes used around the electrodes. We have also, for the first time, been able to locate the seat of potential in such cells, which has been an unsettled question every since the discovery of the battery by Galvani and Volta, at the close of the last century.

The theory of electrolytic dissociation was not applied to biological problems as early as to chemical and physical. This is probably due to the greater complexity of those phenomena in which life is involved. But a beginning has already been made in this direction. Kahlenberg and True have shown that the toxic action of a number of acids on a certain plant, is due to the hydrogen ions of the acids, and similarly the toxic action of a number of bases can be ascribed to the hydroxyl ion of the base.

Loeb has found that the power of a frog's muscle to absorb water in the presence of acids, is dependent upon the number of hydrogen ions present,—upon the dissociation of the acid.

The pharmacologists have actively employed the theory of electrolytic dissociation in the solution of a number of problems. In this connection the work of Dreser is especially to be mentioned, and the theory has also been extended to problems in disinfection, by Paul and Krönig.

The applications of the theory of electrolytic dissociation above considered, are but a very few, taken from a large number where its significance has been already recognized. While it has suggested much new experimental work in several branches of chemistry, and in the study of the electromotive force of elements, yet, it seems to me, that perhaps its greatest service thus far to science has been in correlating facts, pointing out relations hitherto unobserved, and thus leading us from unclassified to at least partly classified knowledge. This has resulted, in a number of cases, in wide-reaching generalizations. We are thus led one step nearer to the solution of the question, not simply how do substances behave in the presence of one another, but why do the phenomena observed take place?

CHEMICAL LABORATORY, JOHNS HOPKINS UNIV.

LOCALIZED SCLEROSES OF THE AORTA OF PROBABLE SYPHILITIC ORIGIN. CLINICAL REPORT AND NECROPSY IN TWO CASES.

By Clement A. Penrose, M. D., *House Medical Officer, The Johns Hopkins Hospital.*

At the request of Dr. Osler I presented (February 7, 1898) to the Medical Society the clinical report and necropsy in a case of circumscribed or nodular arterio-sclerosis of probable syphilitic origin and located quite definitely in two portions of the aorta. Since then we have been fortunate enough to obtain the notes in a second case, that died recently in the hospital, and showed also a well localized sclerosis of the aorta of a circumscribed or nodular type, less advanced and with an even more positive etiology of syphilis.

Case I. J. K., age 36, married, white, an American, a barber by trade, was admitted Tuesday, Jan. 4, 1898, to ward F of the Johns Hopkins Hospital.

Family History. As a child had measles, mumps, whooping cough, and pneumonia. At 19 thought he had syphilis; remembered a primary sore, but could give no definite history of secondary symptoms or treatment. One year later an attack of gonorrhœa. Malarial fever at 24, and at 29 acute rheumatism, with a second attack one year ago. When a young man was a sailor, worked hard, and was not infrequently drunk.

Present Illness. Was well and strong until Nov. 1897, when symptoms of non-compensation of the heart, shortness of breath, palpitation, œdema, etc., set in acutely, and increased in severity up to the time of admission.

Physical Examination. A well-nourished, strongly built man, with symptoms of marked aortic and mitral insufficiency and the corresponding physical signs. Of *especial interest* is a roughened first heart sound in the second right interspace, pronounced dyspnœa relative to other symptoms, absence of any hardening of the radials, for the most part a normal or subnormal temperature, with comparatively slow rate of pulse and respiration (average 90 and 25 per minute), and lastly, a poor reaction to treatment.

The patient improved somewhat, left the hospital 12 days after admission to arrange some private matters, was away one week and returned in about the same condition as on first entry. He gradually sank, and died Jan. 24, 1898, with Cheyne-Stokes respiration for one hour, and slight convulsive movements for a few minutes before death.

Autopsy. The following conditions were found: a slight insufficiency of the aortic valves as indicated by the water test; an absence of vegetations on any of the valves, which were normal, except for a slight thickening and shortening of one of the aortic segments, and considerable hypertrophy with some dilatation of the heart confined chiefly to the left ventricle. The heart muscle on section showed exquisite fatty degeneration, with here and there fibrous areas.

Of special interest was a circumscribed or nodular form of sclerosis, localized in two portions of the aorta, one patch of which involved the ascending and transvere sections of the arch and gave rise to an aneurismal dilatation about the size of one's fist (12 cm. long by 17 wide) extending posteriorly and to the right, containing no blood clots. The walls of the aorta in this region presented a rough, uneven surface; no atheromatous or calcareous degeneration was visible.

The descending portion of the arch and thoracic aorta were practically free from sclerosis until a point was reached a short distance above where it pierces the diaphragm. Here a second patch of sclerosis was found extending down about 8 cm. to the cœliac axis, showing diffuse thickening with nodular elevations especially well marked about the openings of the intercostal arteries.

Microscopical examination showed considerable round cell infiltration and degeneration of the media, interrupting here and there the course of its muscle fibres, with marked irregular thickening of the intima. In places there was some round cell infiltration of the adventitia also. Dr. Flexner in one section found a rather suspicious nodule of epithelioid cells in the media, suggesting a gummatous formation.

Case II. J. R., age 35, single, colored, a laborer, admitted Feb. 2, 1898, to Ward M.

Family History. Negative.

Personal History. None of the diseases of childhood. At 25 had rheumatism, and has had one or two attacks since. Gonorrhœa at 27. He denied syphilis, but showed on corona of penis a well defined, elevated scar about 1.5 cm. in diameter, which seemed fairly recent. He drank moderately. Was not a hard worker.

Present illness began four months ago with shortness of breath, palpitation and œdema, which have been growing steadily worse.

Physical Examination. Strong, well-nourished man, presenting symptoms of aortic and mitral insufficiency with corresponding signs. Dr. Osler, in a note made Feb. 26th, called attention to the wiry character of the systolic murmur in the mitral area, the development of a Flint murmur just outside the nipple, and to the moderate grade of sclerosis of the arteries.

The patient slowly sank, and died quietly, March 3, 1898. His average pulse rate was 104, his respiratory 24, and his temperature 99.5° F.

Autopsy. The heart was much enlarged, both ventricles hypertrophied and dilated. The aortic valve was insufficient to the water test and showed on examination a diffuse thickening with shrinking of the anterior and posterior coronary segments, the intercoronary segment being fairly normal.

The aorta just above the lesion in the valve was the seat of an irregular patch of atheroma, 3 by 4 cm. in diameter, which extended into the sinus of Valsalva of both the anterior and posterior segments and from there out on the valve. The aorta appeared slightly dilated at the portion of the arch where the sclerosis was situated. The anterior and posterior coronary arteries showed yellow patches of atheroma along their course, but no evidences of calcification or occlusion. The aorta

generally was free from atheroma excepting a few yellow patches scattered here and there over the intima.

Microscopical examination of the patch of sclerosis showed marked round cell infiltration of the media, which in places appeared to be quite broken up, the muscle fibres being separated by an œdematous cellular tissue. The adventitia was also considerably infiltrated with small round cells, but the vasa-vasorum showed, however, little change. Nowhere were any definite gummatous nodules found, although a number of sections were examined.

In addition specimens of the chancre scar were examined which showed marked thickening of the epithelium, with an elevation above the surrounding coronal tissue and much subepithelial granulation tissue formation, but no especial vascular changes.

On consulting some of the authorities as to the significance of these localized arterio-scleroses one is impressed with their unsatisfactory classification from a clinical point of view.

Accepting Dr. Councilman's division of arterio-scleroses into the nodular or circumscribed, the diffuse and senile forms, we scarcely know where to place those cases in which both nodular and diffuse scleroses coexist, or cases in which the lesions are definitely localized, at least macroscopically. In addition many writers seem to confuse the term nodular or circumscribed with localized, the former applying more properly to the small nodular elevations or compensatory thickenings in the vessel wall than to the sclerosis as a whole.

It was necessary therefore to look up the subject of localized sclerosis under each one of its etiological factors in the various works at hand, and chiefly under the heading of syphilis, thinking it to be the most probable agent in the two cases under consideration. Forms of localized inflammations and degenerations in arteries arising from local influences such as injuries, burns, skin diseases, tuberculosis and leprosy, fade so gradually into those general arterial conditions arising from general influences such as gout, rheumatism, hard-work and alcohol, that, midway, we find a group of cases very hard to classify.

Syphilis demonstrates remarkably in its different stages this transition from *the local changes* in the arteries in the region of a primary chancre and in various secondary phenomena, up to the later *general arterio-scleroses* of the tertiary period; while intermediate are cases similar to the two reported, where the conditions causing the sclerosis seem general but which present a more or less localized manifestation.

Thoma says we must discriminate between the effects of the luetic virus and disturbances in nutrition caused by lues, when considering arterio-scleroses.

George Thibierge says: "The sclerosis of syphilis is less diffuse than that due to other causes, is more localized, shows often a marked proliferating endarteritis and periarteritis, and is occasionally associated with the formation of gummata containing epithelioid cells and giant cells."

Ziegler says: "Nodular scleroses have a greater tendency to be localized," and later he shows that syphilitic sclerosis tends to be nodular.

Neumann says: "Syphilitic arteritis tends to be nodular."

Chiari described a typical endarteritis obliterans in a child 5 months old, dead from congenital syphilis, and suggests this as an etiological factor in obscure cases of arterio-sclerosis.

Oettinger cites cases of localized arterio-scleroses following acute infective diseases, but occurring in cases under 20 years of age, and quotes Parrot, Andral and Crisp.

Many of the authors, Nasse, Cornil, Huchard and others, show that in tuberculosis we have well localized arterio-scleroses in arteries of the lung and brain.

Heubner says: "Luetic sclerosis begins as a subendothelial growth and later invades the adventitia."

Baumgarten and Lancereaux say: "It starts first in the lymph vessels of the adventitia and later attacks the intima."

Arthur Ernest Sansom says the great pain in certain cases of syphilitic arterio-sclerosis is due to the especial involvement of the adventitia, which has a more abundant nerve supply. He quotes Huchard, who said 35 out of 150 cases of angina pectoris gave a luetic history. He shows that the most pronounced cases of aneurism of the aorta among young persons or among those in the prime of life, were due to syphilis, and that prostitutes for this reason are affected with aneurism of the aorta much more frequently than other classes of women. He quotes Karl Malmsten of Stockholm, who said 80 per cent. of his cases of aneurism were luetic, and Aitken, who said 50 per cent. of soldiers thus afflicted gave a syphilitic history, 5 per cent. a gouty and 5 per cent. a rheumatic.

Welch says that the nodular forms of arterio-sclerosis or endarteritis deformans are limited to the aorta and larger arteries.

Osler thinks that the points of origin of the large branches of the aorta are more prone to undergo sclerotic changes and hence form aneurisms.

Huchard in a very satisfactory manner, in his elaborate article on arterio-sclerosis, sums up his conclusions regarding the effects of syphilis on the arterial system as follows:

Local scleroses are only a beginning of a general condition, as is shown by the microscope, and he quotes Duplaix, who says "General sclerosis is always found by those who look for it." The chief characteristics of syphilitic sclerosis are:

(1) It is nodular and not diffuse.

(2) It has a tendency to invade portions only of a vessel-wall.

(3) Its onset is usually chronic, but it may be acute.

(4) The points of attack in order of frequency are:

1. Cerebral arteries.
2. Aorta—especially ascending portion of arch.
3. Arteries of heart.
4. Arteries of pericardium.

(5) It has a tendency to obliterate vessels.

(6) It has a tendency to form aneurisms.

(7) In analogy with tuberculosis it has a tendency to obliterate arteries, to form aneurisms, and to become localized.

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FURTHER REMARKS ON ADENO-MYOMA OF THE ROUND LIGAMENT.

By Thomas S. Cullen, M. B. (Tor.), *Associate in Gynecology, Johns Hopkins University.*

In the May-June number of the Bulletin, 1896, I reported a case of adeno-myoma of the round ligament, the first on record. Since that time three cases bearing on the same subject have occurred, and our own case has revealed some very instructive etiological factors.

Pfannenstiel* reports the case of an unmarried woman, 39 years of age, who had long been suffering from dysmenorrhœa, and who came under observation on account of a tumor in the right inguinal region which had made its appearance about six months previously. On examining the patient a nodule was also found in the vagina; this Pfannenstiel supposed was the primary tumor, and inferred that the nodule in the inguinal region was a metastasis. The uterus and its right appendages, together with the nodules in the inguinal region and vagina, were removed. The vaginal nodule on section presented the picture of a myoma, but scattered throughout it were yellowish-brown dots of pigment, and it contained fine depressions and cysts. On histological examination the tissue was found penetrated in all directions by glands, and in their cavities were pigment granules, and in one place a pseudo-glomerulus was found. The nodule from the inguinal region was scarcely the size of a walnut. It was situated a short distance within the external ring and presented the same picture as the vaginal nodule. In short, Pfannenstiel says there was a simultaneous appearance of adeno-myoma at two different points in the genital tract. He identifies his case with the same group as the one reported by us.

v. Herff† examined two vaginal myomata removed by Fehling during a hysterectomy for prolapsus uteri. One of these contained numerous delicate glands, some of which were branched and slightly dilated, others formed small cysts. These glands lay as little islands in the musculature. The gland epithelium was either cuboidal or low cylindrical. At no point could a comb like arrangement of the glands or the pseudo-glomeruli of v. Recklinghausen be demonstrated.

Blumer's* case, 47 years of age, had first noticed the growth 23 years before coming under observation. At that time it formed two distinct nodules, each about 6 mm. in diameter, in the right groin. These gradually coalesced and the combined tumor grew slowly until six months ago, since which time it rapidly increased in size, being at the operation as large as a hen's egg. The growth had never been painful, even at the menstrual period. Dr. Van der Veer, who removed the tumor, believed that it originated in the inguinal canal.

The tumor was firm in consistence, greyish-white in color, and contained pin-point hemorrhages; in most points it resembled an ordinary uterine myoma. Histological examination showed that the tumor was composed mainly of non-striped muscle fibres, and in one section gland elements were found. These appeared round or oval, but occasionally as dichotomously branched spaces. The gland epithelium was cylindrical and contained oval, darkly staining nuclei; in some places cilia could be seen. The glands were in direct contact with the muscle, there being no stroma intervening, and Blumer was unable to find any structures resembling pseudo-glomeruli or to make out any sign of pigmentation.

Our patient (Gyn. No. 5286) was readmitted to the gynecological ward, May 25, 1897. Shortly after the previous operation she noticed a swelling in the opposite or left inguinal region immediately above the pubes. This has gradually increased in size and is quite painful. The menstrual period has not been regular, occurring at intervals of from three to five weeks. The last menstruation commenced May 18th and ceased May 23d. On May 26th I removed the nodule with little difficulty and found that it was directly continuous with the left round ligament.

Pathological report. Gyn. Path. No. 1741. The specimen consists of an irregular mass approximately 3 cm. in its various diameters. It comprises a firm central portion 1.5 cm. in diameter, which is surrounded on all sides by adipose

* Ueber die Adenomyome des Genitalstranges. Verhandlungen der Deutschen Gesellschaft für Gyn., 1897.

† Ueber Cystomyome und Adenomyome der Scheide. Verhandlungen der Deutschen Gesellsch. f. Gyn., 1897.

* A Case of Adeno-myoma of the Round Ligament. American Journal of Obstetrics, 1898, XXXVII, p. 37.

tissue. Traversing the central portion are numerous delicate fibres, and at several points are brown or yellow homogeneous areas. Several pin-point cavities are demonstrable. At one point is a semicircular slit 2 mm. long, and in the immediate vicinity an irregular cavity averaging 3 mm. in diameter. The walls of this cavity are rather uneven and are slightly granular.

Histological examination. The adipose tissue in the outlying portions is comparatively normal, but as one approaches the firm nodule the blood-vessels increase in number and size, young capillaries are found wandering in between the fat cells, and there is considerable connective tissue increase, the fat cells becoming gradually separated from one another. At the margin of the firm nodule the tissue is composed almost exclusively of connective tissue. Here and there this connective tissue encircles round or oval clumps of cells having oval, fairly deeply staining nuclei, and scattered between these are a few small round cells and occasionally polymorphonuclear leucocytes. Such areas are very striking on account of their richness in nuclei, in contrast to the surrounding tissue which is poor in cell elements. The cellular areas resemble closely the stroma of the uterine mucosa. On passing toward the centre of the nodule similar areas are found containing one or more glands lying in their centre or at the periphery. These glands, according to the angle at which they are cut, are round, elongate or slightly branching. Their epithelium is cylindrical, apparently ciliated, and their nuclei are oval and situated some distance from the base of the cell. In short these glands cannot be distinguished from uterine glands. The majority of the gland cavities are completely filled with blood and desquamated epithelial cells. The stroma of the central portion of the nodule is composed almost entirely of non-striped muscle fibres, and here the glands are more abundant and present a more complicated picture. The glands are branching, form narrow channels and little bays, and in places can be traced in their continuity for at least 4 mm. On one side of the gland there is usually considerable stroma separating the epithelium from the underlying muscle. At such points the epithelium is cylindrical, but on the opposite side where the cells rest directly on the muscle it is frequently flattened. There are a few areas corresponding to von Recklinghausen's pseudo-glomeruli; some of these contain glands, others do not.

Origin. Even from such a small number of cases we are able to gather valuable information as to the distribution of these tumors. In v. Herff's case the nodule was limited to the vagina, Blumer's to one inguinal region, while Pfannenstiel's contained two nodules, one in the inguinal region and a second in the vagina, and in our case nodules were found in both inguinal regions. This apparently varied distribution seems nevertheless to follow definite channels, viz. the round ligament on one or both sides, and it will be little wonder if in later publications reports of adeno-myomata near the uterine end of the round ligament will be recorded.

Pfannenstiel and v. Herff mention nothing as to any definite relation between menstruation and the nodule, but Blumer states that menstruation in no way affected the nodule in his case. When publishing our case I drew attention to the excessive pain in the nodule at the menstrual period, suggesting some definite sympathetic relation between the uterus and the nodule in the round ligament.

Two sources of origin for these tumors have been suggested, viz., from a displacement of a portion of the Wolffian body or from a part of Müller's duct. v. Recklinghausen has very kindly examined sections from the nodule removed from the right round ligament in our case and thinks that it is undoubtedly of Wolffian origin. v. Recklinghausen,* after seeing Pfannenstiel's and v. Herff's specimens, says that these also are of Wolffian origin. When publishing our case I made the following remark: "While admitting the probability of the glands in our case being due to remains of the Wolffian body, we cannot, from their striking resemblance to those of the uterine mucosa, and from the fact that their stroma resembles that of the mucosa, refrain from suggesting the possibility that they may be due to an abnormal embryonic deposit of a portion of Müller's duct." In this connection the relation of the last menstrual period to the presence of blood in the glands is interesting. Menstruation commenced May 18th, ceasing May the 23rd, or just three days before operation, and on making sections the glands were found filled with well preserved blood. In adeno-myomata of the uterus and also of the round ligament, blood or blood pigment is met with in the gland cavities in the gland epithelium or in the underlying stroma. If these glands be derived from a portion of Müller's duct we would naturally expect them to fulfil, at least in part, the functions of the normal uterine mucosa, viz., furnish their quota of blood at the menstrual period. Under the existing conditions, however, this blood cannot escape and will be gradually taken up by desquamated cells lying in the gland cavity, by the epithelium or by the stroma cells. In our case the blood was not perfectly fresh, but the corpuscle outlines were still intact. This is what might be expected, assuming that the hemorrhage had occurred at the menstrual period. I am still more inclined to favor the Müllerian origin than heretofore.

Prognosis. Our case was of eight years' duration, and on histological examination gave no signs of malignancy, showing that the growth was benign in character. Blumer's case is even more convincing, as it had been followed for 23 years, the growth in that time not becoming larger than a hen's egg, and on microscopic examination also showing its harmless character.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

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* Personal communication.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of February 21, 1898 (*continued*).

Regeneration of the Dorsal Root of the Second Cervical Nerve within the Spinal Cord.

Messrs. BAER, DAWSON and MARSHALL.—The present work was undertaken in order to determine whether it is possible to obtain regeneration of the nerve fibres within the spinal cord, and these studies were confined to the regeneration of the dorsal-root fibres after their continuity had been destroyed between the spinal ganglion and the cord.

The second cervical nerve of the dog was selected for the experiments, because the spinal ganglion of this nerve lies outside the intervertebral foramen. The dorsal root can, therefore, be operated upon much more readily and with less danger of injuring the cord than would be the case if it were necessary to open into the vertebral canal. There were, also, reasons connected with the histological work which made it advisable to select the second cervical nerve.

The two roots of this nerve pass together to the ganglion 2 mm. beyond the foramen, the trunk then subdividing to supply muscular and cutaneous branches to the neck and base of skull. The occipitalis magnus, with which we are chiefly concerned, courses through the neck muscles and beneath the skin, to end in the integument behind the ear. The second cervical is connected with the sympathetic, not by a mixed ramus communicans, but by a gray ramus alone.

The present article deals only with the physiological results; the histological studies will be completed at a later day. Our method of investigation included two operations. At the first, the roots of the second cervical were tightly ligated, so as to destroy the continuity of the dorsal-root fibres and cause them to degenerate throughout their extent in the cord. The animals were kept alive long enough to allow regeneration to follow the degeneration.

At the second operation the nerve was tested for return of function of the dorsal root. Such a return would be indicated by reflex variations in respiration, blood pressure and pulse rate, which might follow stimulation of the nerve in question.

As control experiments, kymographic tracings were obtained from two normal dogs, showing the reflex changes due to stimulating the second cervical nerve.

At the first operation the occipitalis magnus was followed through the muscles and exposed as far as the cord. The roots were freed from surrounding tissue, a ligature was passed around them and tied tightly, great care being taken to avoid exerting traction upon the cord. The ligature was then cut away, leaving a constriction plainly visible at the point of ligation; the two parts of the nerve being united only by a tube of translucent connective tissue—the epineurium—while the continuity of the enclosed fibres was destroyed. In every case the wound healed per primam.

The interval between the first and second operations was about 90 days, the two longest intervals being 109 and 151 days.

At the test for regeneration a canula was inserted into the carotid artery and connected with a mercury manometer which was made to record upon a kymograph. Similarly the trachea was connected with a tambour which was arranged to give a kymographic record. A time recorder and a stimulating or short-circuiting key also recorded upon the kymograph, so that the tracings were made to give four simultaneous records, that of circulation, respiration, time, and duration of stimulation.

Scar tissue rendered dissection more difficult than previously, but the nerve was exposed as at the first operation and stimulations were applied at various points along the occipitalis magnus, upon the ganglion and upon the roots. Stimulations were of two kinds, faradic and mechanical. The current was never of greater strength than sufficient to cause slight pain when the electrodes were touched to the tongue, and for the most part a weaker current was used. Mechanical stimulation consisted in crushing the nerve with forceps or a ligature.

The results obtained upon the several dogs may be summarized as follows:

In the two normal dogs, used as controls, every stimulation of the second cervical nerve was followed by marked increase in the frequency of pulse and respiration, increased amplitude of respiration and a rise of blood pressure; these being the usual reflex effects of stimulating a sensory nerve.

In dog I, every stimulation caused increased amplitude of respiration, rise of blood pressure, and usually, but not always, a quickening of pulse and respiration.

In dog II, stimulation of the ganglion and roots caused an increase in the amplitude and rate of respiration and a rise of blood pressure. The pulse rate showed practically no reflex change.

In dog III, faradic stimulation at the ganglion and mechanical stimulation of the occipitalis magnus caused a rise of blood pressure, with an increase in the rate and amplitude of respiration. The pulse rate was affected variably and to only a slight degree.

Dog IV responded less to stimulation than any dog of the series. Respiration was unaffected throughout. The pulse rate and blood pressure showed reflex variations for the first three stimulations of the occipitalis magnus, after which there was no sensory reflex present.

Dog V gave positive but diminished changes after stimulation in respiration, blood pressure and pulse rate.

Dog VI responded very slightly, but gave both respiratory and cardio-vascular reflex changes.

In the case of dog VII very positive reflex changes were obtained. Blood pressure was greatly affected, while the respiratory reflex was tremendous.

From a study of the above experiments it appears that a more or less complete return of function occurred in every

case, although the reflex effects were very slight in dogs IV and VI. Such an apparent return of function might be produced in several ways.

1. By failure to destroy the continuity of all the dorsal-root fibres at the first operation. The following facts contradict this assumption. After obtaining the usual effects from stimulating the second cervical nerve of a normal dog, the roots were ligated in the usual manner. Subsequent stimulation produced no effect. Again, after giving the routine stimulations to dog III, with positive results, the roots were again ligated. Subsequent stimulation was without effect, and microscopical examination showed a complete break in the continuity of the fibres at the point of ligation.

2. The apparent return of function might be due to anastomosis with neighboring nerves. But the above-mentioned controls on dog III and a normal dog show that although the finer ramifications of the second cervical anastomose with neighboring nerves, it is not possible for impulses to pass from a branch of the second cervical to the cord through these connections.

Again, escape of current to the cord might be assumed to account for the apparent return of function, but that this was not the case is shown by the positive results of mechanical stimulation of the nerve. Moreover, in every case the nerve was dissected out and retracted from the surrounding tissues before the electrodes were applied, and in some cases positive results were obtained from stimulation with weak currents applied at the extreme periphery of the occipitalis magnus about 6 cm. from the ganglion. In the case of the ganglion, where retraction was impossible, many of the stimulations, especially with strong currents, were accompanied by control stimulations of the surrounding tissues, and always with negative results.

We are left, then, with but one explanation of this return of function, which is, that the reflex effects were produced by impulses passing through the dorsal root of the nerve stimulated, that is to say, through the dorsal root of the second cervical nerve.

Such a return of function could occur in only one of two ways. Either the root may be regenerated from fibres having their trophic centers within the cord, or else the regeneration may proceed from trophic centers outside the cord. From a study of the literature it is a justifiable conclusion that all the fibres of the dorsal root of the second cervical nerve in the dog spring from centers outside the cord. Therefore, any return of function of the injured dorsal root is proof of regeneration of the injured fibres both in the root and within the cord itself.

As we have seen, there was return of function in every animal experimented upon, though the degree of restoration varied in the different cases.

Owing to the limited number of our experiments we have been unable to determine how complete regeneration may be, and how it is influenced by varying conditions.

After the first few days the animals did not appear to suffer inconvenience from the first operation, nor was there any evidence of trophic disturbance over the area supplied by the injured nerve.

The completeness of functional return appeared to depend very little upon the length of the interval between the first and the second operations. The most complete return of function occurred in dogs I and VII, with an interval between the operations of 90 days and 109 days respectively. The lowest degree of regeneration was seen in dogs IV and VI, with intervals of 90 and 151 days respectively.

We could not determine how the power of regeneration is affected by the age of the animal selected for experimentation. Of the only two adult dogs operated upon, one (dog I) gave marked reflexes, the other (dog IV) gave only slight evidence of regeneration.

There is, however, one condition, namely, scar tissue around the nerve, which exerts an unfavorable influence upon regeneration. This action has been frequently discussed by other observers, and we consider that the successful regeneration of the dorsal-root fibres in these cases has been due, in great measure, to the fact that the new growth of the fibres was not interfered with by the presence of excessive scar tissue; the operation employed reducing to a minimum the cicatricial tissue at the growing point of the nerve. In only one case, dog VI, was the spinal ganglion affected by scar tissue. Here the ganglion was distorted and bound down by adhesions, and, correspondingly, the sensory reflexes were very slight in this case.

From the experiments described above we feel justified in concluding that, after severance of the fibres of the dorsal root of the spinal cord, between the ganglion and the cord, regeneration of the fibres into the cord will take place under suitable conditions, so that normal reflexes upon the respiratory, cardiac and vaso-motor centers may be obtained.

Finally, we wish to thank Dr. Howell for his many valuable suggestions and the interest which he has taken in our work.

DISCUSSION.

Dr. BARKER.—This study, if confirmed, and it seems likely that it will be confirmed, includes results of importance not only for the physiologist and anatomist but also for the clinician. It leads us to hope that regeneration within the central nervous system may occur much more extensively than has hitherto been thought possible. It is true that most investigators believe at present that destruction of cells within the central nervous system means a permanent loss, since the opinion is general that there can be no regeneration of ganglion cells once destroyed. There have been two researches, however, recently, one by Vitzou and another by Tedeschi, on regeneration of nerve cells in the cortex of monkeys after extirpation. The results of these experiments, though worthy of note and control, by no means justify the extravagant enthusiasm which has been manifested by certain lay journals. The problem in the research reported to-night, however, is somewhat different, inasmuch as the regeneration of nerve fibres alone is postulated, not the regeneration of total neurones.

In connexion with this study of Messrs. Baer, Dawson and Marshall we shall await with interest the results of the histological examination. It is necessary that the return of fibres within the dorsal root and within the cord itself shall be

histologically demonstrated, although from the physiological experiments reported there can be but little doubt that this proof will be easy to bring forward.

Mr. MARSHALL.—With Dr. Barker, we look forward with great interest to the histological findings in the cases just reported, but we are, nevertheless, of the opinion that the physiological evidence is weightier and of more positive value than the histological.

When the experiments were undertaken, I may say, it was our intention to complete both the physiological and histological sections before making public our results. But the former method yielded results which were so unequivocal that we felt justified in publishing the physiological work alone, in the belief that the histological studies could be only confirmatory.

Hydraulic Pressure in Genito-Urinary Practice.—Dr. H. H. YOUNG. [See May BULLETIN, p. 100.]

Dr. RUSSELL.—At the request of Dr. Kelly I will briefly report the following case of cystitis treated in his private hospital by Dr. Young's method. The case, although not one of contracted bladder, shows the value of this method in the treatment of cases of chronic cystitis where the ordinary irrigation and drainage have failed. Mrs. L. F. D., age 32, five years ago, after an instrumental labor, had a severe attack of acute cystitis, and since then there has been almost constant bladder trouble. She cannot hold her urine longer than two hours, day or night, and usually the interval is much less. Urination is nearly always attended by severe pain, and occasionally she loses control over the bladder. Three years ago she had Emmet's button-hole operation, which gave relief during the eight months the bladder was drained, but as soon as the fistula was closed the old trouble returned. Pus has been present in variable quantity during this time, and occasionally blood. Once there was quite a free hemorrhage from the bladder. Her husband has been washing out the bladder through a catheter, which has given temporary relief.

February 25, 1898.—An examination revealed a complete tear through the perineum and an acutely retroflexed uterus. The bladder on the posterior surface was deeply reddened, but no vessels were seen. In the left lower quadrant was a deposit of white lymph and mucus intimately adherent to the surface beneath it. The vault of the bladder was mottled with red injected areas, and absolutely no vessels could be seen. The affection was most severe at the base of the bladder, which was covered with extensive greyish deposits, the largest area being on the left side at the junction of the wall and base, covering an area about 3x3 cm. The left ureteral orifice appeared as a little point in the midst of a white area. These greyish areas had irregular margins covering shallow ulcers of the mucous membrane. The only trace of sound mucosa was about the internal orifice of the urethra.

The bladder was then thoroughly curetted by a sharp curette, and about 2 oz. of a twenty per cent. solution of silver nitrate was injected, followed immediately by a pint of normal salt solution.

Two days later Dr. Young's method was employed, the irrigation being given every two hours. After two weeks the improvement was so marked that the number of irrigations was dropped to intervals of four hours.

March 16th.—On account of some return of pain the patient was again examined under ether. The change in the local condition was astonishing; in every direction the mucous membrane had returned to normal, except at the left and base of bladder. This area has the same appearance as previously described and bleeds easily on touch. These points were again curetted and an application of silver nitrate made. The intervals between the irrigations were then reduced to six hours.

March 23rd.—A continuous steady improvement has been noted since the Young method was adopted. The patient now goes four to six hours frequently without voiding urine and sometimes sleeps all night. Several times during the past ten days the patient has been able to hold 500 cc. of solution during irrigation. The urine, which upon admission was loaded with pus and mucus and was always strongly alkaline, is now at times slightly acid and has only a small sediment.

Forty-six Intubated Cases of Diphtheria treated with Antitoxine.—W. T. WATSON, M. D.

Of the 46 cases reported, 37 recovered and 9 died, giving a mortality of 19.5 per cent.

The recovered cases were of all grades of severity, from the cases in which the constitutional symptoms were slight and the children lively and playful as soon as the laryngeal stenosis was relieved, to those in which there was such profound prostration that for days life was despaired of. In some cases the tube was coughed up in two or three days and did not have to be replaced; in others it had to remain in for two weeks, and in one instance for 22 days. In the earlier cases the tube was allowed to remain in place for a week, unless coughed up or taken out to be cleaned. In the later cases, according to the practice of O'Dwyer, the tube was removed in four days and reinserted if necessary.

In some cases the nourishment was entirely liquid; in others, particularly the later cases, the children were given anything they would take, liquid or solid, of a wholesome character.

Only in one case, where for two days the patient was unable to swallow, was nasal feeding found necessary.

The amount of antitoxine in the earlier cases was almost invariably 1000 units; in the later cases the initial dose was usually 1000 units for a child under two years and 2000 units for children of two and over. It was usually given just after intubation.

The diagnosis was confirmed by culture, by membrane in the pharynx or which came up from the larynx during or after intubation, or by the presence of diphtheria in other members of the family.

Particular attention was paid to a study of the nine fatal cases. In at least four of them death was due to neglect, the children being in a practically moribund condition when intubation was performed and antitoxine administered. In one case, an infant of 11 months, the tube became blocked with a tough piece of membrane and the baby immediately suffocated. One died of broncho-pneumonia four days after the tube had been removed and the laryngeal symptoms had disappeared.

The other three cases received antitoxine and were intubated reasonably early, but died with symptoms of lung complication.

The death-rate from laryngeal diphtheria before the advent of intubation was almost 100 per cent. After the introduction of intubation it fell to about 75 per cent. At present with the antitoxine treatment some cases do not require operation, but in the operated cases the death-rate has fallen to about 27 per cent.

This death-rate is far too high and will be much reduced in the future when physicians are more impressed with the importance of the early use of antitoxine and early operation to relieve stenosis.

Intubation should be performed upon the first advent of dyspnœa. In some cases where the dyspnœa is slight the amount of mucus which will escape from its imprisonment below the glottis, during and after intubation, is often surprising. If this mucus is allowed to accumulate for many hours it is possible that it might be the means of conveying infection to the lungs and setting up a broncho-pneumonia.

DISCUSSION.

Dr. FLEXNER.—The last point made by Dr. Watson, that of the release of the bronchial mucus and its expectoration, impresses me as very important. We know now, thanks to the studies of Wright and Kanthack and Stephens, that the secondary pneumonias of diphtheria are caused in the majority of instances by the Klebs-Loeffler bacillus, and are not pyococcal in origin as was formerly believed. Dr. Anderson and myself have also been able to show that intratracheal inoculation of pure cultures of the bacillus diphtheriæ in rabbits provokes a pneumonic process. The bronchial and tracheal mucus contains the diphtheria organisms, and often in large numbers, so that its aspiration into the lung substance is to be prevented as far as possible, in the hope of averting the lobular pneumonias which so often are the immediate cause of death.

Dr. WATSON.—In determining to intubate every case where the first signs of dyspnœa appear I am led to do so because no harm can result from it. It is painless, bloodless, and can do nothing but good.

I think, too, that intubation should be done by the general practitioner. He sees these cases first, and sometimes the parents have already delayed the matter too long, and in some cases by the time the physician has arranged to secure the services of a specialist, the child is dead, or at least it is too late for it to recover. I recently had a case where the child died a few minutes after intubation just from exhaustion; it had been struggling for breath for 24 hours. I have been called to three cases within the last year and a half where the children were dead before I arrived, and I know that others in this city have had similar experiences. When the general practitioner becomes qualified to intubate the death-rate of laryngeal diphtheria will be greatly lowered.

HOSPITAL PLANS.

Five essays relating to the construction, organization and management of Hospitals, contributed by their authors for the use of The Johns Hopkins Hospital.

These essays were written by DRS. JOHN S. BILLINGS, of the U. S. Army, NORTON FOLSOM of Boston, JOSEPH JONES of New Orleans, CASPAR MORRIS of Philadelphia, and STEPHEN SMITH of New York. They were originally published in 1875. One volume, bound in cloth, price $5.00.

NOTES ON NEW BOOKS.

Die Anaemie. I. Abtheilung. Normale und pathologische Histologie des Blutes. Von Geh. Med.-R. Prof. Dr. P. EHRLICH und Dr. A. LAZARUS. 8vo. *Wien: Alfred Holder*, 1898. [Extract from *Specielle Pathologie und Therapie*. Herausgegeben von Hofrath Prof. Dr. HERMAN NOTHNAGEL. Bd. viii, 1. Theil, 1. Heft.]

The contributions of Professor Ehrlich and his pupils to the study of the blood have been of such great importance that this work has been looked forward to with considerable interest, both by physiologists and practitioners; and neither will be disappointed in their anticipation.

The present volume deals only with the general normal and pathological histology of the blood. The consideration of the pathology of the blood in special diseases will be dealt with in a second fasciculus. In an introduction the clinical methods of blood examination are considered. In discussing the methods of estimation of hæmoglobin the authors justly speak of the value of the very simple clinical test, consisting in allowing a drop of blood to flow upon a piece of white cloth or filter paper, a method which if more used would prevent many a careless diagnosis of "anæmia."

They next take up the *morphology of the blood*, recommending especially the study of dried and stained specimens. The methods of preparing and examining dried cover-glass specimens are thoroughly set forth, and several valuable formulæ are given for the preparation of different staining solutions; that for the preparation of the *triacid* stain is of particular value as a distinct improvement over the previously recommended methods.

The section upon the *normal and pathological histology of the blood* begins with the consideration of the red blood corpuscles The well known idea of Ehrlich as to the manner of origin of poikilocytosis (schistocytosis) and its conservative significance is reiterated. The question of the manner of origin and significance of the different varieties of nucleated red corpuscles is then discussed in a most interesting manner. The authors maintain that the disappearance of the nucleus takes place in the normoblasts by extrusion, in the megaloblasts by fragmentation and absorption. These latter elements they have found only in pernicious and in bothriocephalus anæmia. The megaloblastic degeneration of the bone marrow is believed to be due to chemical influences of unknown origin.

The section upon the colorless corpuscles is, as might have been expected, one of great interest and importance.

The function of the spleen with regard to blood formation is considered at length. The conclusions reached from the work of Kurlov and others—that the spleen is of little importance as a producer of colorless corpuscles—that if cells be produced in the spleen, these are non-granular elements—that its function in this respect is more similar to that of the glands than to that of the bone-marrow—that "the spleen has not the least relation to ordinary leucocytosis," seem to be abundantly justified.

The fact that the glands are the seat of origin of the lymphocytes is clearly brought forth, and great emphasis is laid on the fact that no sufficient proof has yet been advanced that these cells have any genetic relation to the ordinary polymorphonuclear leucocytes. They form, according to the authors, a totally distinct and separate class of elements. This conclusion is in sharp contradistinction to that of the school of Uskov, who have assumed that the cellular elements of the blood have a distinct genetic relation to one another, the lymphocytes representing the youngest forms, the polymorphonuclear neutrophiles the fully developed or "old" elements, an attractive but hardly justifiable view.

It is interesting to note that the authors deny positively the power of lymphocytes ever to emigrate from the blood-vessels.

The bone marrow is shown to be the point of origin of those blood cells possessing specific granulations, neutrophilic, eosinophilic and basophilic (Mastzellen). The possible origin of the eosinophiles from fixed tissue cells is doubted. Beside being the

point of origin of the majority of the leucocytes in the blood, the bone marrow is regarded as a storehouse for the polymorphonuclear neutrophiles, from which, by chemotactic influences, they may be called forth in great numbers. 'Leucocytosis is a pure function of the bone marrow." In the section on the "*Demonstration and significance of the granules*" the original view of Ehrlich that these elements represent specific metabolic products of the cell is maintained. The granules of the cellular elements of the blood are believed to be truly specific; but one variety of granule ever appears in a single cell. The common idea that eosinophilic and basophilic granules may occur in the same cell is believed by Ehrlich to be due to misinterpretation of a staining reaction which may occur in young imperfectly developed eosinophilic cells, where some of the granules may for some time show a more or less well marked basophilic tendency. This color reaction is, however, always distinct from the sharp metachromatic stain taken by the true Mastzellen granulations. There is, the authors believe, some evidence that under circumstances the substance of the granules may become dissolved and escape from the cell. In conclusion they say: "In general the granules of the wandering cells are capable of being given off into the neighborhood. This elimination is possibly one of the important functions of the polynuclear leucocyte."

Leucocytosis is divided into an *active* and a *passive* form according to whether the cells increased in the circulation are incapable of individual movement and appear in answer to chemotactic irritants, or whether they are elements without locomobility which are washed passively into the circulation by mechanical influences. The type of the active form is represented by the ordinary polymorphonuclear leucocytosis; of the passive, by conditions of lymphæmia.

The active leucocytoses are separated into:

"(*a*). Polynuclear leucocytoses:

(1) Polynuclear neutrophilic leucocytosis.

(2) Polynuclear eosinophilic leucocytosis.

(*b*). Mixed leucocytoses in which granular mononuclear elements take part: 'Myelæmia.'"

The leucocytosis of the death agony is believed to be due solely to circulatory changes; the slowing of the current is followed by an accumulation of the leucocytes along the walls of the vessels. The polynuclear neutrophilic leucocytosis is considered, as has been said before, to be purely a function of the bone marrow, dependent upon chemotactic substances calling forth the neutrophilic cells from their storehouse. The authors also believe that in most instances the substances positively chemotactic for the neutrophilic cells act in a negative manner toward the eosinophiles; hence the small number of the latter cells in ordinary leutocytoses. All active leucocytoses are not, however, of chemotactic origin. In some forms an increased activity of the bone marrow or an extensive change of fatty into red marrow may be the exciting cause.

The various conditions under which the *polynuclear eosinophilic leucocytosis* occurs are next considered. The authors are strongly of the opinion that the eosinophilic leucocytosis depends also upon chemotactic causes, other, however, than those calling forth the polynuclear leucocytosis. They do not believe in the local origin of eosinophilic cells elsewhere than in the bone marrow, nor do they agree with those who believe that the eosinophilic granules may arise from a direct transformation of the neutrophilic elements, a view which, it is but fair to say, has considerable in its favor, especially the remarkable observations of Brown in trichinosis. They believe that these chemotactic substances, while in some cases—for instance, in helminthiasis—foreign to the organism, are, for the most part, the products of some tissue destruction in the body itself. Attention is drawn to the remarkable relation between the presence of Charcot's crystals and the increase in eosinophilic cells

The section upon *leukæmia* is extremely interesting. With justice, apparently, the authors insist that, from an hæmatological standpoint, there exist but two forms of leukæmia:

"(1). Leukæmic processes associated with an hyperplasia of lymphoid tissue: 'Lymphatic leukæmia.'

"(2). Leukæmic processes associated with hyperplasia of myeloid tissue: 'Myelogenous leukæmia.'"

Lymphatic leukæmia is divided into an acute and a chronic form. The increase in the number of lymphocytes is believed to be due to a passive washing out into the blood, not to an active emigration due to chemotactic influences.

Myelogenous leukæmia is discussed at length and an admirable description of the elements is given. "The microscopical picture of myelogenous leukæmia, apart from the almost invariable extensive increase in the colorless corpuscles, is conspicuous for its extremely variable and changeable character. This results from the association of various anomalies, namely:

A. Beside the polynuclear cells and their forerunners, the mononuclear granular leucocytes circulate in the blood.

B. All three types of the granulated cells, neutrophiles, eosinophiles and mast-cells, take part in the increase in the colorless corpuscles.

C. Atypical cell-forms appear; for instance, dwarf forms of different varieties of colorless corpuscles, and, moreover, mitotic figures.

D. The blood always contains nucleated red blood corpuscles, often in considerable numbers."

Attention is called to the constancy of the *absolute* increase in the number of eosinophilic cells in leukæmia, one of Ehrlich's original observations which every competent observer has been able to confirm.

Emphasis is also laid on the constant increase in the number of mast-cells in this disease. This is a point which, so far as we are aware, has been little emphasized and yet one of considerable importance. The authors justly remark that the mast-cells may be recognized as well in specimens stained with the triacid mixture as with the characteristic stains for basophilic granules, inasmuch as they are here represented by polynuclear non-granulated elements. We believe that in many instances it is possible to actually distinguish the non-stained granules in such specimens.

The nature of myelogenous leukæmia is discussed in an interesting manner, and the conclusion is reached that the "origin of the leukæmic blood picture is to be explained by the assumption that, under the influence of the specific leukæmic poison, not only the ripe polynuclear elements but also their mononuclear eosinophilic as well as neutrophilic forerunners, wander into the blood; that, therefore, myelogenic leukæmia is in all probability to be classed among the active leucocytoses."

The diminution of the leucocytes observed experimentally preceding leucocytoses, and believed by Loewit and others to be due to an actual destructive process (*leucolysis*), is thought to depend rather upon a negative chemotaxis. Attention is, however, called to the true *leucopenia* which may exist in some grave anæmias, dependent apparently upon a lack of activity of the bone marrow.

The authors speak guardedly with regard to the nature of the blood platelets as well as of the *hæmokonion* of Mueller.

The volume is a clear and direct statement of the views of the foremost living authority upon changes in the blood; it is an extremely valuable addition to medical literature. It is to be hoped that the second part will be soon forthcoming. W. S. T.

BOOKS RECEIVED.

Operative Gynecology. By Howard A. Kelly, A. B., M. D. Vol. I. 1898. 4to. 563 pages. D. Appleton & Co., New York.

Manual of Operative Surgery. By H. J. Waring, M. S., M. B., B. Sc. (Lond.), F. R. C. S. 1898. 12mo. 661 pages. Young J. Pentland, Edinburgh, and The Macmillan Co., N. Y.

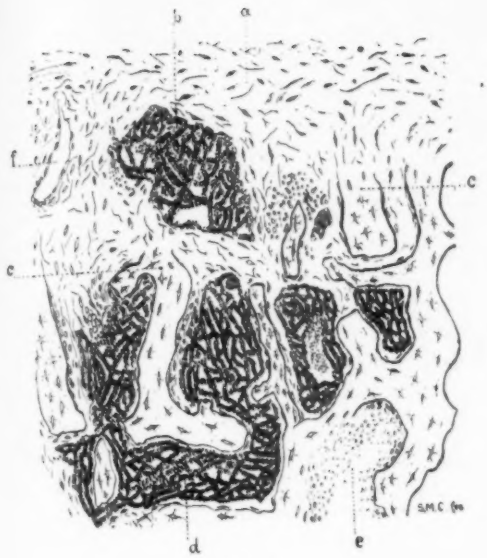

FIG. 1.

FIG. 2.

NOTE.—This plate is intended to accompany Dr. Cone's article in the May number. To face p. 118.

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LOUIS E. LIVINGOOD, M. D., Assistant in Pathology.
HENRY BARTON JACOBS, M. D., Instructor in Medicine.
CHARLES R. BARDEEN, M. D., Assistant in Anatomy.
STEWART PATON, M. D., Assistant in Nervous Diseases.
NORMAN MCL. HARRIS, M. B., Assistant in Pathology.
HARVEY W. CUSHING, M. D., Assistant in Surgery.
J. M. LAZEAR, M. D., Assistant in Clinical Microscopy.
J. L. WALS, Ph. G., Assistant in Pharmacy.

GENERAL STATEMENT.

The Medical Department of the Johns Hopkins University was opened for the instruction of students October, 1893. This School of Medicine is an integral and coördinate part of the Johns Hopkins University, and it also derives great advantages from its close affiliation with the Johns Hopkins Hospital.

The required period of study for the degree of Doctor of Medicine is four years. The academic year begins on the first of October and ends the middle of June, with short recesses at Christmas and Easter.

Men and women are admitted upon the same terms.

In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.

2. Graduates of approved colleges or scientific schools who can furnish evidence: (*a*) That they have acquaintance with Latin and a good reading knowledge of French and German; (*b*) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the colleges or scientific schools where they have studied, as to the courses pursued in physics, chemistry, and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school, will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

ADMISSION TO ADVANCED STANDING.

Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

SPECIAL COURSES FOR GRADUATES IN MEDICINE.

Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, bedside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

The Annual Announcement and Catalogue will be sent upon application. Inquiries should be addressed to the

REGISTRAR OF THE JOHNS HOPKINS MEDICAL SCHOOL, BALTIMORE.

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